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THE HISTORY OF THE DISCOVERY AND ISOLATION OF THE MALE HORMONE

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THE first knowledge of testicular function was acquired empirically by the ancients when domestic animals were castrated for various reasons. However, the specific effects in men were also familiar to those early civilizations where eunuchs were a part of the social order. Furthermore, the *Áyurvéda*, by Susruta of India,[1] written about 1400 B.C., recommended the administration of testicular tissues for the cure of impotence. From these times until within the past twenty years, with the exception of very few animal experiments in the middle of the eighteenth and nineteenth centuries, the knowledge of the secondary functions of the gonads did not advance much beyond the facts known in the Middle Ages.

With some degree of overlapping, the investigation of the endocrine functions of the testes may be grouped with a certain fitness into the following periods: speculative and observational; experimental; and analytic and synthetic.

SPECULATIVE AND OBSERVATIONAL PERIOD

The customs of primitive people and society until rather recent times dictated forms of organotherapy and the use of organs as medicine, such as the eating of hearts from animals, or even from man, to encourage bravery, or the use of brain as food to counteract idiocy. Perhaps it was for such reasons that the ancients and the people of the Dark Ages indulged in organotherapy, especially of such substances as bile, blood, bones, dung, brains, feathers, horns, intestine, placenta, reproductive organs and teeth. Often the difficulty of obtaining a part was its most attractive attribute. Nothing was too disreputable for use. *Dreck Apotheken* specialized in secretions and excretions,[2] but other books, especially Heberden's[2] *Antitheriaka* (1745), discredited these disgusting preparations. It is interesting to note that today many of the sex hormones, including that of the male, are obtained from human waste products.

The type of therapy employed by medieval physicians is an indication of their conception of the nature and cause of disease. At a time when disease was treated according to a jumble of mysticism, philosophy and dogma, critically appraised concepts of the action of even the exocrine glands could not be formulated. There are some physiologic statements which in the light of modern knowledge show glimpses of suspected fact. A vague foreshadowing of the endocrine function of the testis can be found in the works of Aretaeus,[3] the Cappadocean (*ca.* 150 A.D.), in the chapter on gonorrhea: "For it is the semen, when possessed of vitality, which makes us to be men, hot, well braced in limbs, well voiced, spirited, strong to think and act. For when the semen is not possessed of its vitality, persons become shrivelled, have a sharp tone of voice, lose their hair and their beard, and become effeminate, as the characteristics of eunuchs prove." Rolleston[4] mentioned that Johannes Mesuë, the Elder (777–837), prescribed testicular extracts as an aphrodisiac and against pulmonary tuberculosis. Some real understanding of the problem was first voiced in 1775 by Théophile de Bordeu, a graduate from Montpellier and a physician at the court of Louis XV. He was the founder of the theory of vitalism, and strove to show that the humoral pathology of Hippocrates was due to bodily secretions. For many organs and their secretions he enumerated specific diseases. In this manner he arrived at the concept that each organ of the body produces a substance which enters the blood stream and that the sum total of these forces regulates bodily functions. He even cited the well-recognized underdevelopment of secondary sexual characteristics in eunuchs, capons and spayed female animals in connection with the absence from the blood of specific secretions of the gonads. In his book, *The Medical Analysis of Blood*, he[5] came to the con-

clusion that "each [of these organs] is a store room and laboratory for a particular humor [substance] which is given off into the blood after it has been prepared in its bosom [that is, the organ], and has thus conferred upon it [the humor] a radical [specific] character."

These views are very similar to those expressed by Brown-Séquard,[6] and are practically identical with the modern definition of endocrine function. Speaking of testicular secretions, de Bordeu[7] stated: "I accept as fully demonstrated medically the view of such continuous emanations from each organ into the blood. And if we take into consideration the facts discovered by anatomists with regard to the existence of the lymphatics, I would say that the gelatinous liquor [that is, the semen of the testis] is sent into every organ of the body by certain vessels, and confers upon the chyle in the thoracic duct the properties and peculiarities of the 'ingredients' of which they are composed." He believed that the gross structure of the cellular tissue was the chief site of exchange of these secretions, since the true dimensions of the lymphatic network were still incompletely known. No one prior to Berthold,[8] or even Brown-Séquard, visualized as closely as did de Bordeu the true mode of action of the endocrine glands. Neuberger[9] in 1911 emphasized the approximation of de Bordeu's speculation to the mechanism of internal secretions by ductless glands. Yet others consider the uncritical writings of de Bordeu as an attempt to classify cachexias resulting from various secretions, excretions and organs in a none too discerning fashion. Garrison,[10] in the "History of Endocrinology," writes: "The book is a typical example of the purely theoretical reasoning so common in the medical literature of the eighteenth century, in which an intolerable deal of verbiage is spread over the smallest substructure of fact." He regarded the sexual secretions as giving "a male — or female — tonality" to the organism, "setting the seal upon the animalism of the individual." Observations regarding castration, known to animal-breeders since much earlier times, were confused by him with hearsay reports and anecdotes, and did not induce him to test his ideas experimentally. The historian must remain on guard so as not to read modern concepts into fanciful hypotheses.

During this period of speculation, some progress was made in the study of the anatomy and physiology of the ductless glands. Aristotle, in his *Historia Animalium*, written prior to 300 B.C., described the testes and ovaries in many species of animals and showed a clear conception of the effect of castration. In book nine of the fourth volume he[11] wrote: "If the bird be full-grown [when castrated] his crest grows sallow, he ceases to crow, and foregoes sexual passion; but if you cauterize [that is, castrate with hot irons] the bird when young, none of these male attributes or propensities will come to him as he grows up. The case is the same with men; if you mutilate them in boyhood, the later-growing hair never comes, and the voice never changes but remains high-pitched; if they be mutilated in early manhood, the late growths of hair quit them except the growth in the groin, and that diminishes. . . ."

While the knowledge of secretions of the testes, other than the semen, gradually evolved, the study of glands in general, and of the ductless glands in particular, formulated many fundamental principles that applied to all internal secretions. Galen knew of the existence of the pituitary gland, although Vesalius[12] described it first in 1543 and named it after the Latin word *pituita*, meaning "mucus" or "phlegm," — which, as both believed, was secreted by it. Schneider[13] in 1655 and Lower[14] in 1670 proved that such mucus did not pass from the brain to the nose, and suggested an internal secretion of this gland. Willis[15] in 1664, according to Rolleston,[16] believed that "the blood poured out something — through the spermatic arteries to the genitalia — and that it received in turn certain ferments from these parts, — that is, certain particles imbued with a seminal tincture and carried back to the blood, — which makes it vigorous and instills into it a new and lively virtue."

Gley[17] claimed that Legallois[18] in 1801 had come more closely to the concept of internal secretion than had de Bordeu. Legallois found that although arterial blood was of the same composition throughout the body, venous blood varied considerably, depending on the site from which it was obtained. This difference he attributed to the fact that the organs removed something from the blood, which then passed into the veins. This claim is scarcely as impressive as that of Willis and of Lower.

Thus, in less than half a century, ductless glands were recognized as closely allied to the vascular system and capable of secreting a substance into the blood stream. The close association with the blood vessels was pointed out by Broussais[19] in 1817 for the spleen and the adrenal, thyroid and thymus glands, and by Béclard[20] in 1823 for the pituitary and pineal glands. Johannes Mueller[21] in 1834 and Henle[22] in 1841 differentiated between glands with and without ducts, and believed that the ductless glands changed the composition of the blood.

One may say that ancient and medieval scientists formulated certain philosophical theories on glandular secretions. These hypotheses, when read

from a modern point of view, seem to indicate in many instances a fair comprehension of the presence and function of the endocrine secretions, especially those of the testis. Such an assumption, however, is pure inference, and these concepts may not have been so clearly formulated in the minds of the philosophers, who based their conclusions on a few casual observations.

Experimental Period

Many centuries had passed since Aristotle ascribed pubertal changes to the function of the gonads, as such manifestations were absent in castrates. In the era of enlightenment, objective study was combined with sound reasoning by many anatomists and scientists, until John Hunter and Berthold approached the problem experimentally. John Hunter[23] in 1762 attempted to ascertain whether the genital organs of one sex could be grafted to and grow in the body of the opposite sex. He transplanted the testicles of a cock into the abdomen of a hen, and in several cases found that some grafts had taken root there, but "did not come to perfection." For this reason he considered the experiments as incomplete and of no value. However, he failed to mention any "masculinization" effects observed with the few successful transplants.

In 1848, Berthold,[8] then professor of physiology in Göttingen, removed the testes of four roosters and replaced one testis in an unusual abdominal position in each of two capons. He killed these two capons six months later, and found that because of the testicular grafts "these animals remained male in regard to voice, reproduction instinct, fighting spirit, and growth of comb and wattles. . . . The *consensus* [that is, the interrelation of function among different parts of the body] is maintained by the productive influence of the testicle; that is to say, by its effect upon the blood, and through the blood, upon the organism."

Berthold's clear and important demonstration of endocrine secretion was published in a five-page paper which remains the only noteworthy epitaph of an author who wrote voluminously on other subjects. Rudolf Wagner,[24] the physiologist, could not confirm Berthold's findings in 1850, and the influence of the discovery was almost forgotten until Biedl,[25] in his monograph *The Internal Secretions*, resurrected the work and bestowed on Berthold "the honor of having first proved the existence of an 'internal secretion' and of having recognized its significance."

By 1850 the long-recognized influence of the testis had been demonstrated to be caused by blood-borne secretions of these ductless glands. These facts were disregarded, however, and it was only after impressive experiments in the field of metabolism that inferences were drawn regarding endocrine organs. Great progress followed the work of Claude Bernard,[26] who in 1843 proved that cane sugar is changed to dextrose by gastric juice. These results became widely known, and as Garrison[27] remarks regarding internal secretions, "It was the fact that glycogen [Bernard's *sécrétion interne* of the liver] could be seen, touched, tasted and experimented upon, as such, that established the theory of internal secretions as a working principle in physiology."

At the time of Bernard's studies, Thomas Addison[28] extended to the adrenal gland the principle of glandular hypofunction, which had been recognized for centuries with regard to the testes, but had not been known to apply to the other glands. His classic description of the disease of the adrenal glands that now bears his name was verified within a year by Brown-Séquard,[29] who extirpated the adrenal glands and found that the animals showed the symptoms described by Addison.

The latter part of the nineteenth and the early part of the twentieth century was a period in which general principles were outlined. Bernard had formulated the concept, *la fixité du milieu intérieur*, or the constancy of the internal environment, by which he meant that higher animals maintained a constancy of temperature and bodily fluids. It became known that the endocrine system, in conjunction with the nervous system, especially with the autonomic portion, aided greatly in maintaining the remarkably even tenure of involuntary bodily activities.

A slight digression is in order for the purpose of tracing the development of the fundamental nomenclature of endocrine secretions. According to Rolleston,[30] the term "internal secretion" was first used by Claude Bernard in a lecture at the Collège de France on January 9, 1855. Speaking of his work in glycogenesis, Bernard said that the liver had an "external secretion" of bile and an "internal secretion" of sugar, which passes directly into the general circulation.

Bayliss and Starling,[31] in 1903, believed that the term "internal secretion" inadequately expressed the widespread action on the body as a whole of chemical entities produced in certain organs, and transported elsewhere by the blood and the lymphatics. Starling,[32] in the first Croonian Lecture before the Royal College of Physicians, on June 20, 1905, spoke of "the chemical messengers or 'hormones' [I excite or arouse]." According to Rolleston[33] this word was suggested by W. B. Hardy after consultation with W. T. Vesey from Caius College, Cambridge.

In the early years the selection of the term "hormone" was frequently criticized on the ground that it applied by definition only to substances that have a stimulating action, and failed to include those that had an inhibiting or depressing effect. Yet Jayle[34] stated that this word or its derivatives had already been used by Hippocrates. Likewise John Smith,[35] a physician from Brasenose College, Oxford, used it in his *Gaerokomia Basilikae*, when he spoke of the "hormetick power and concentration" of the muscles. Schäfer,[36] in his book, *Endocrine Organs*, suggested the term "hermone" (from Hermes, "messenger"), which would exclude any ambiguity and could be applied to both stimulating and depressing agents. In 1913, he[37] had already advanced the term "chalone" ("I loosen") for the inhibitory hormones and the word "autocoid" ("self-remedy") as a generic name for all internal secretions, and reserved the noun "hormone" exclusively for stimulating agents. The use of these terms, however, did not become popular, and is at present largely discontinued.

Pende,[38] an Italian, had introduced the term "endocrinology" ("I separate within") in 1909, while Gley,[39] a Frenchman, suggested the term "harmazone" ("I regulate") for the morphogenetic and growth-controlling secretions of the gonads and thyroid and pituitary glands at the International Congress of Medicine in London in 1913. The word "parahormone" was chosen to denote metabolic products, such as carbon dioxide, which act like hormones at a distant site.

Ironically, after a period of brilliant experimentation, clinical endocrinology was introduced by the uncontrolled study and blatant claims for rejuvenation in 1889 by Brown-Séquard,[6] who at the age of seventy-two injected himself with aqueous extracts of the testes. He claimed as results an improvement in general health, muscular strength and appetite, and regulation of the intestinal tract and mental faculties. He[40] even suggested orchitic extracts as a panacea and advised their use, for example, in tabes dorsalis.

Preparation and critical investigation of extracts were logical steps in this practical period of endocrinology, and Brown-Séquard's statement of the principles involved was essentially correct. Garrison[41] summarizes Brown-Séquard's ideas as follows:

> All the tissues, in our view, are modifiers of the blood by means of an internal secretion taken from them by the venous blood. From this we are forced to the conclusion that, if subcutaneous injections of the liquids drawn from these tissues are ineffectual, then we should inject some of the venous blood supplying these parts. . . . We admit that each tissue, and more generally, each cell of the organism, secretes on its own account certain products or special ferments, which, through this medium, influence all other cells of the body, a definite solidarity thus being established among all the cells through a mechanism other than the nervous system. . . . All the tissues [glands or other organs] have thus a special internal secretion and so give the blood something more than waste products of metabolism. The internal secretions, whether by direct favorable influence, or whether through the hindrances of deleterious processes, seem to be of great utility in maintaining the organism in its normal state.

This is the theory of de Bordeu, restated at a stage in the development of science when accrued knowledge permitted more precise formulation. The preceding quotation shows beyond doubt that Brown-Séquard clearly believed that the endocrine glands liberate active substances into the blood stream. This passage is markedly different from his views in 1855, when he[29] stated that extirpation of the adrenal glands permitted accumulation of pigments in the blood, these pigments becoming poisonous in the absence of detoxification by the glands.

The unfortunate parts of Brown-Séquard's work were the uncritical manner of investigation and the extravagant claims of rejuvenation. With the possible exception of the search of Ponce de Leon, the ageless quest for perpetual youth was never brought so closely and so attractively to the attention of the world. The limitations in the technics of grafting of the testes and in administration of testicular extracts were overlooked. Much of his so-called therapy was useless and unapproved by competent contemporaries or successors of Brown-Séquard. The susceptibility of many minds in matters pertaining to sex and the false hopes raised by extravagant claims led inevitably in a pendulum fashion to a viewpoint strongly antagonistic to the acceptance of the efficacy of any testicular substances, an opinion well warranted until the last few years. Early experiences with inactive ovarian mushes and dried matter increased the skepticism concerning the usefulness of gonadal preparations (Novak[42]). The inevitable result was that strong prejudice for and against a mode of therapy has been built not on controlled observation and experimentation, but on wishful conclusions, inactive preparations and useless grafting operations. When active chemical substances of known, measurable and stable potency were prepared in 1936, there was already a great superstructure of largely discrediting data purportedly related to the method of substitution therapy, but in actuality proving not that the principle is incorrect, but that the technics previously utilized in substitution therapy were inadequate. This distinction must be made between the use in human beings of testicular grafts or extracts in contrast to

the present-day employment of crystalline compounds.

The unsavory aroma of attempts at rejuvenation did not prevent rapid advances in clinical endocrinology. It is interesting to speculate on the course of events had Brown-Séquard tried his theory of autotherapy in hypothyroidism instead of in attempted rejuvenation. Yet his work in attracting world-wide attention encouraged trial of substitution therapy in states of deficiency resulting from the poor functioning of other glands.

Overactivity of the endocrine glands, by the nature of the phenomena involved, was a matter appreciated more slowly than were deficiencies in glandular activities. The testis, the gland in which hypoactivity and endocrine secretion were first demonstrated, is not known to produce any striking sequelae of hyperactivity. Precocious sexual development is occasionally seen with interstitial tumors of children, but the condition of masculinity is not known to exceed the stage seen in normal men.

Although principles were formulated and rapid progress made in investigation of other endocrine glands, the study of testicular function advanced slowly, and on many fronts there was only a marking of time. Interrelations with other glands, particularly with the pituitary, were clearly demonstrated by studies of these glands, notably in the work of Rathke,[43] Fröhlich,[44] Cushing,[45] Evans[46] and Smith.[47]

In 1908–1910, some of the details of the castrate condition in men were supplied by Tandler and Grosz[48] in a series of studies of the Skoptsy, a religious sect whose members inflicted self-mutilation according to the following advocation in the Bible:

> For there are some eunuchs, which were so born from their mother's womb: and there are some eunuchs, which were made eunuchs of men: and there be eunuchs, which have made themselves eunuchs for the kingdom of heaven's sake. He that is able to receive it, let him receive it. (Matthew xix:12.)

Additional and significant data concerning the action of male hormone substances were gleaned by animal experimentation with grafting and other manipulation of the testes (Lipschütz[49]), but unhappily some studies bore the connotation of rejuvenation. A history of research of male-hormone substances would be incomplete without some mention of attempts at rejuvenation.

A chief drawback to the accomplishment of rejuvenation lies in the fact that aging affects the structure and function of cells in a manner not reversible by sex hormones. Not all cells can be expected to be restored to a status compatible with an earlier age. The use of the term "rejuvenation" (Steinach[50]) deserves severe indictment, even if applied solely to the genital organs, for the changes induced by androgenic stimulation are scarcely a "re-establishment of youthfulness." It is of fundamental importance to realize that aging occurs in various degrees in different cells, and only wishful thinking can glibly circumvent the obstacles opposing any rejuvenation merely by secretions of the testicle, even if the secretions resemble those existent when the individual was younger. It is not inappropriate to recall that in the immature boy, youth prevails without the prodding of large amounts of testicular secretions.

To those with scientific inquiry were added searchers, not of facts, but for means whereby the testis would become the fountain of youth. Charlatans reaped a financial windfall. The chief methods employed to obtain testicular secretions were implantations of a testis from another man or beast, the injection of extracts from animal testes and the stimulation to secretion of the testes already existing.

Transplantations of the testis involve a number of problems, especially satisfactory vascularization and compatibility with the environment provided by the host. Despite any excellency of operative methods, it is held in some quarters to be almost axiomatic that grafting in mammals should be to a host of the same species. Testes from goats, monkeys or other animals have not proved to have satisfactory survival and function after transplantation to man. Persistence of a mass of tissue at the site of implantation is in itself not assurance that the graft has "taken," for microscopic examination may reveal only fibrous tissue remaining. Even within the same species successful grafting is enhanced by inbreeding. Although many transplants of testes have been made from one man to another, the results have been poor, a fact not astounding in view of the difficulties of obtaining specimens in good condition, a sufficiently close relation between donor and host and a suitable endocrine status in the host. Some of the men receiving grafts have been eunuchoids in whom gonadotropins may have failed to stimulate the individual's own testes and in whom the pituitary rather than the testes have been primarily responsible for the eunuchoidism. From the standpoint of reproductive purposes, it should be noted that even if interstitial elements in the graft were to persist, the seminal epithelium would be less likely to grow satisfactorily.

Attempts to stimulate the testes of an individual can be accomplished in certain cases by the administration of gonadotropic substance. Claims have also been advanced, but without general acceptance, that testicular secretions can be augmented

by ligation or resection of the vas deferens. The theoretical basis of such operations is that the interstitial tissue is the source of androgens; that blocking of the seminal duct near the testis causes destruction of the seminiferous epithelium, presumably because of pressure; and that when the seminal epithelium is destroyed there is an increase in interstitial cells, and therefore more hormone is produced.

The period of experimentation occupied about a century and a half. Work, at first sporadic and haphazard, progressed slowly and was often misinterpreted. Berthold, about one hundred years ago, conducted experiments under the strictest control, the significance of which was fundamental and is still unimpeachable. However, the blatant claims of Brown-Séquard discouraged further advances, even though the extracts produced by him may be considered as the first attempts to isolate the male hormones. Subsequent workers advanced the knowledge of endocrinology as a whole and devised a fundamental terminology. However, the unwarranted claims of rejuvenation propounded by Steinach and by Voronoff as results of testicular grafts had the same effect as the claims of Brown-Séquard had on the studies of Berthold.

Analytic and Synthetic Period

Progress in the preparation of testicular-hormone extracts was slow. The lack of suitable methods for assay and the absence of adequate resources for male-hormone substances became evident, especially when compared with the high titers of female hormone found in the urine of pregnant women and domestic animals. The numerous experiments of earlier investigators indicated at least one testicular hormone, but efforts to isolate it remained futile for many years.

The discovery by Pézard[51] in 1911 of the capon as a quantitative biological test animal for androgens was a fundamental step forward. Pézard injected extracts from the testes of crypt-orchid pigs twice weekly for five months into a cockerel that had been castrated two months earlier and showed castration atrophy, and found that one tenth of a cryptorchid hog testis would produce an increase in the size of the comb and the wattle of this capon as compared with similar control birds. However, the omission of detail in his report prevented repetition and confirmation of his experiments.

McGee,[52] in 1926, working in the laboratory of Koch in Chicago for his doctor's dissertation, was the first to prepare a lipoid extract from fresh bull's testes, 0.01 mg. of which would restore the atrophic comb of a capon. He thus confirmed an endocrine function of the testis. Three years later Loewe and Voss,[53] of Mannheim, reported before the Academy of Sciences in Vienna that an extract obtained from 3.6 liters of urine from normal men would restore the castration effects of the seminal vesicles of a mouse.

Moore and his collaborators,[54–58] of Chicago, in a series of studies, investigated for many years the physiologic action of testicular extracts, and not only defined the rat unit but also performed tests on spermatozoon motility, on electric ejaculation in guinea pigs and on the cytology of the prostate, the seminal vesicles and the vas deferens of the rat. Heller,[59] in 1930, studied the effects on Cowper's gland, and Binet and Luxembourg,[60] of Paris, in 1939 found that the female Xiphophore, an aquarium fish, produced a characteristic male caudal fin when injected with male urine twice weekly for six weeks. Moore and Price,[61] in a classic study, presented the most adequate exposition of the interrelations between the anterior-pituitary gland and the testes.

During these years progress was rapid. In 1931, Butenandt,[62] of Danzig, succeeded in isolating in crystalline form 15 mg. of two chemically pure substances, "androsterone" and "dehydroandrosterone," from 15,000 liters of male urine by the Funk–Harrow[63] method. He found that these substances were sterols of the probable formulas, $C_{16}H_{26}O_2$ or $C_{19}H_{30}O_2$, and that they were closely related to the female hormone "estrone." Ruzicka and his associates,[64] at the Polytechnic Institute in Zurich, were impressed by the similarity of Butenandt's formula for androsterone to that of cholesterol. They attempted to produce, and promptly succeeded in doing so, a synthetic crystalline compound of the same formula as Butenandt's androsterone. They evolved the process which is now used for the commercial synthesis of androsterone and testosterone by the degradation and hydrogenation of epicholestanol.

At about the same time, chemists were engaged in the laboratory of Laqueur in Amsterdam in similar work. In 1935, David et al.[65] announced the isolation of a crystalline substance, "testosterone," from bull's testes, just before Ruzicka's laboratory[66] synthetized it. This testosterone was many times more potent than the androsterone of Butenandt, and differed from it chemically by the reduction of the keto radical at carbon atom 17. Up to the present time more than thirty substances of male-hormone character, but of different degrees of physiologic activity, have been prepared synthetically by the degradation of sterols. Essentially there are two types, a saturated and an unsaturated series. Koch,[67, 68] in 1937 and in 1939, has given the most comprehensive exposition of the chemistry of these androgenic substances. The

following excerpt will best convey the chemistry involved:

> A consideration of androsterone and its closest isomeres . . . shows that the *cis* configuration of the OH on carbon atom 3 with reference to the H on carbon 5 is very important providing the H on carbon 5 is *trans* to CH_3 on carbon 10. If the H on carbon 5 is *cis* to the CH_3 on carbon 10, as it is in the derivatives from coprosterol and epi-coprosterol, the physiological activity is negligible. The importance of the configuration about carbon 3 is again shown when the 17-keto group is reduced as in the androstanediols. Note that reduction of the 17-keto group in androsterone and trans-androsterone (dehydro-iso-androsterone) increases the potency. In other words, the 17-position secondary alcohol group is even more important than the 3-epi-OH (3-*trans*-OH) form in determining potency. If both 3 and 17 positions are oxydized to ketones, as in androstanedione, there is not much change from the androsterone potency.
>
> The discussion above covers the saturated series. In the unsaturated series the conversion of the 17-keto group into a secondary alcohol may alter the activity slightly, but not as much as in the saturated series. . . . Comparison of the unsaturated with the saturated di-ketones does not reveal a striking effect unless the unsaturated group is between carbons 1 and 2; then the unsaturation produces a striking loss of potency. . . . Conversion of carbon 17 into a tertiary alcohol with the –OH kept *trans* also increases the potency somewhat. It appears then that the most favorable arrangements for high potency known thus far are found in testosterone and 17-methyl (*cis*) testosterone.[68]

Male hormones and their derivatives are therefore sterols related to those found in the bile acids, adrenal cortex, cardiac glucosides and the digitalis sapogenins. They are closely related to some vitamins and to the carcinogens. Androgenic substances have been isolated from urine, feces and the adrenal glands. The urine of normal men and women contains androsterone and dehydro-iso-androsterone (Tscherning[69] and Butenandt and Tscherning[70]) in rather large quantities as compared with the low titers found in the tissues.

Although male hormone was isolated and synthetized in a comparatively short time, there was not such progress in the determination of its sources in the testicle. The interstitial cells, first described in 1850 by Leydig,[71] then professor of histology at Würzburg, and since identified by his name, are commonly believed to be the elements that produce this hormone. This view was first advanced in 1896 by Reinke,[72] who described certain crystalloids in these cells, now known as the "Reinke crystalloids." Ancel and Bouin[73] from 1903 on devoted numerous papers to the study of these cells. They introduced the term "interstitial gland" to denote the secretory function of these cells, and argued strongly in favor of their being the source of male hormone. Steinach,[50] in 1912, coined the name "puberty gland"; he[74] believed that it not only secreted the androgens, but could also be rejuvenated by vasoligation, a concept which became very popular for many years. Bouin,[75] in 1931, advanced additional evidence to prove that the interstitial cells were the producers of the testicular hormone.

This hypothesis, however, has been greatly contested, and is still not generally accepted. Furthermore, McCullagh, alone[76] in 1932 and with his associates[77] in 1935, presented some evidence that the testis may also secrete a second hormone, "inhibin," which inhibits the activity of the pituitary gland. Although the presence of the inhibin principle has been denied by some authorities, there still remains some good evidence in its favor. However, further experimental studies are needed to settle this question, which is mentioned here merely for its historical interest.

* * *

In conclusion, it can be stated that the testis was the organ first suspected of, and associated with, an internal secretion. It was likewise the first gland subjected to animal experimentation. Yet, in spite of this, approximately a century — from 1848 until 1935 — was needed before the androgenic hormone was isolated and synthetized in pure crystalline form. This fact is still more surprising when comparison is made with the internal secretions of other glands, such as the thyroid, the parathyroid, the pancreas and the adrenals, whose endocrine activity was not suspected until much later, yet whose active principles were isolated chemically, and even synthetized, much earlier than were those of the testis.

With the chemical isolation and synthesis of the androgens a period has been reached in which they are studied in relation to the general metabolism of the body and to the other endocrine glands, especially the pituitary and the adrenal cortex, and in which they are applied therapeutically in several clinical syndromes. This work already commands a huge literature, but concepts are still indefinite and need more study to permit final conclusions.

In order to recapitulate the history of the discovery and isolation of male hormone, it is appropriate to present the high lights of this interesting chapter of endocrinology in a chronological tabulation:

1400 B. C.	The *Âyurvêda* of Susruta recommends testis tissue as treatment for impotence.
460–370	Hippocrates uses the word "hormone" for certain ferments.
384–322	Aristotle describes castration effects in birds, beast and man.

40 A. D. Matthew mentions in his Gospel eunuchs made by God (congenital) and by man (castrated), and thus furnishes the basis for the self-mutilation of the Skopets sect of Russia.

150 Aretaeus, the Cappadocean, in his description of gonorrhea suggests that the semen is the basis of the characteristics of the male.

131–201 Galen of Pergamus knows of the pituitary and believes that it secretes a "phlegm" into the nose.

777–837 Johannes Mesuë, the Elder, prescribes testicular extract as an aphrodisiac.

1543 Vesalius describes the anatomy of the pituitary gland and coins its present name.

1664 Willis believes that the blood receives certain ferments from the spermatic veins that make it vigorous and lively.

1666 John Smith uses the word "hormetick" for certain muscular metabolic products.

1745 Heberden's *Antitheriaka* leads to the purification of the "filth" pharmacopoeias.

1762 John Hunter transplants the gonads of one sex into the other sex, but his experiments are not successful.

1775 Théophile de Bordeu argues in favor of internal secretions from some glands.

1801 Legallois finds that venous blood varies according to the organs from which it comes.

1817 Broussais points to the close association of blood vessels with the adrenal, thyroid and thymus glands and the spleen.

1823 Béclard shows the close relations of blood vessels to the pituitary gland and the pineal body.

1834 Johannes Mueller differentiates between glands with and without excretory ducts.

1843 Claude Bernard demonstrates glycogenesis and glycogenolysis as functions of the liver.

1848 Arnold Berthold performs the first successful testicular transplants in capons and thus proves an endocrine function of the testes.

1850 Franz von Leydig describes certain cells in the testis, which are now known as the "Leydig interstitial cells."

1855 Thomas Addison publishes his classic monograph on adrenal disease, known now by his name.

Claude Bernard introduces the term "internal secretion."

1889 Brown-Séquard publishes his famous paper on self-rejuvenation after treatment with testicular extracts.

1896 Reinke describes the crystalloids of the interstitial cells, now bearing his name, and suggests that these cells secrete the male substances.

1903 Ancel and Bouin introduce the term "interstitial gland" to indicate the secretory function of the interstitial cells.

1905 Starling introduces the term "hormone" for all internal secretions, as known today.

1907 Tandler and Grosz describe the skeletal changes found in eunuchs and Skoptsy after prepubertal castration or self-mutilation.

1909 Pende introduces the term "endocrinology" for the science of internal secretions.

1911 Pézard discovers the capon comb and wattle growth as a test for male-hormone determination.

1912 Steinach coins the word "puberty gland" and suggests that it can be rejuvenated by ligation of the vas deferens, a procedure now known as the "Steinach operation."

1926 McGee produces a lipoid extract from bull's testes.

1929 Loewe and Voss produce an androgenic extract from urine.

1931 Butenandt isolates crystalline androsterone and dehydroandrosterone from male urine.

1934 Ruzicka and his assistants synthetize androsterone, and later also testosterone.

1935 David and his associates, in Laqueur's laboratory, isolate crystalline testosterone from bull's testes.

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MILITARY DISCHARGE FOR INADEQUACY*

Report of 182 Cases

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CAMP BLANDING, FLORIDA

MEDICINE is not yet an exact science. Army induction boards labor under difficulties that frequently increase the margin of error. They are compelled to work under great pressure, the time allotted is sadly inadequate, and there is often a shortage of trained specialists.[1] Moreover, it is impossible in one examination to weed out all those physically and psychically unable to perform as soldiers. Thus, unqualified men are occasionally placed in uniform. Unfortunately, this does not make them soldiers.

Army regulations provide for the discharge from the Service of these unfit persons. Those who fail because of organic disease or from psychoneurosis or psychosis are released under regulations providing for a certificate of disability for discharge.[2] This procedure we have outlined elsewhere.[3]

Under further regulations (so-called "Section VIII cases"),[4] "when an enlisted man (1) is inept, or (2) does not possess the required degree of adaptability for military service, or (3) gives evidence of traits of character or habits which serve to render his retention in the service undesirable, or (4) is disqualified for service physically or in character, through his own misconduct," steps are taken to separate him from the service. This is not done, however, "until every reasonable effort has been made to develop the enlisted man concerned into a soldier." Further, every consideration must be given to the advisability of transferring the enlisted man to another organization of the regiment or post in order that he be given every opportunity to develop into a soldier. This does not apply to enlisted men who show undesirable habits or traits of character.

In most cases the discharge given is the "blue" discharge from the Army of the United States. This is neither honorable nor dishonorable; it is a discharge without honor. Exceptionally, an honorable discharge is given when the conduct of the enlisted man during his enlistment has been such as would render his retention in the service desirable were it not for his inaptitude or lack of required adaptability for military service. In these cases the discharge certificate must show that reenlistment is not warranted. No discharge papers may contain the reason for the discharge.

We have collected all these discharges, issued through the Station Hospital at Camp Blanding, Florida, for its first year, from November 5, 1940, to November 5, 1941.

The military personnel of this camp consisted of two divisions, the Thirty-First or Dixie Division, made up of troops from Florida, Louisiana, Mississippi, Alabama and Georgia, and the Forty-Third or New England Division, made up of troops from Maine, New Hampshire, Vermont, Rhode Island, Connecticut and Massachusetts, the Seventy-Fourth Field Artillery Brigade, composed of National Guard units from Georgia and New Hampshire and of men from the Regular Army, and the Corps Area Service Command troops from varied sources. The average camp population, subject to marked fluctuation, was approximately 30,000, ranging as high as 45,000 and at times dropping as low as 5000.

The total number of men discharged for inadequacy was 182. On the basis of an average camp population of 30,000 this is 0.6 per cent.

The following factors entered into the making of these decisions and must be considered in the appraisal of the statistics. The first factor is the difficulty in making many officers newly on active duty conform strictly to the necessary tedium of Army regulations; for this reason, many such cases have been overlooked. The second factor is the probability that many of these cases have been diagnosed as being due to organic disease. Too many physicians still refuse to recognize the frailty of the psyche because of overconcentration on the weakness of the soma. "If a man says he has a pain, how can you know he hasn't a pain?" Undoubtedly many diagnoses of sacroiliac sprain, mild heart disease, enuresis, flat feet, spastic colon and similar diseases should have been included in this group. And, finally, the board which must recommend discharge is composed of officers from the enlisted man's own company. Too often in National Guard divisions they have known the soldier at home. They are therefore inclined to doubt that he is a psychiatric case, or if they accept the diagnosis, they may be reluctant for personal reasons to discharge him on this ground. For all these reasons we believe that the number of discharges mentioned above is far below the actual number of cases warranting such action.

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‡Registrar, Station Hospital, Camp Blanding (deceased).

Hospital Days of Cases of Inadequacy

The 182 discharged men spent a total of 7405 days in the Station Hospital, for an average of 40.7 days per man. Their hospital admissions totaled 309 (Table 1). In the same period for

Table 1. *Hospital Admissions.*

No. of Admissions per Man	No. of Men	Total Admissions
One	90	90
Two	66	132
Three	19	57
Four	5	20
Five	2	10
Totals	182	309

the entire camp a total of 286,592 hospital days were required for all pathologic conditions encountered; these included an epidemic of influenza and an epidemic of measles. Thus, 2.6

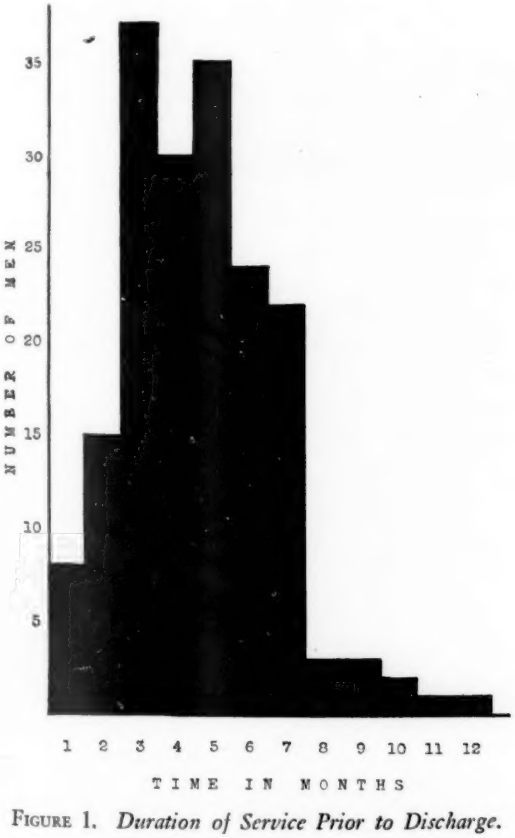

Figure 1. *Duration of Service Prior to Discharge.*

per cent of the total number of hospital days were utilized by the group of 182 cases under discussion.

It must be pointed out that only 16 of the 309 diagnoses with which these men entered the hospital carried any note regarding mental observation. In all other cases the men were admitted for organic complaints. Much of the time lost was on wards where such complaints were investigated and ruled out. The neuropsychiatrist was called in only as a last resort.

Time Required for Recognition of Condition

The period of time from induction until the condition leading to discharge was finally diagnosed varied from five days to eleven months (Fig. 1). It will be noticed that only 10 of the 182 men lasted in the service longer than six months, and that the peak for recognition

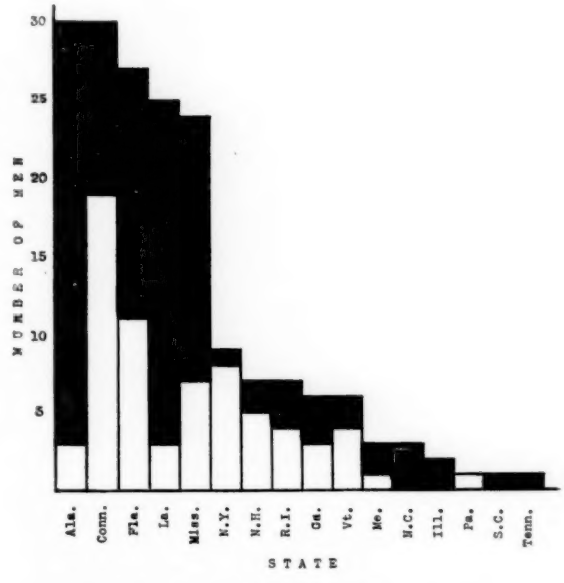

Figure 2. *Geographical Distribution by States.*

The unshaded blocks represent men from urban areas; the shaded ones, men from rural areas.

of the discharge condition was three months. This is probably a longer time than will be needed for recognition in the future. In the formative period of the camp, inept and unadaptable men were not subject to the same strain and surveillance as they will undergo henceforth.

Geographic Distribution of Discharged Men

The discharged men were classified by Army divisions, by states of origin and by their previous environments, rural or urban. The Dixie Division contributed 112 (0.62 per cent) of its total manpower of 17,942 soldiers, the New England Division 53 (0.32 per cent) of its 16,483 soldiers, and other units 17 men. These figures do not seem to reflect any differences in the caliber of the men from various parts of the country. A probable contributing factor was the fact that New England induction boards were somewhat more

efficient in weeding out subnormal material than those in other sections.

On the basis of figures given in the *1941 World Almanac*, we listed all residents of towns of 2500 population or over as urban, and divided the discharges accordingly into rural and urban. We found that 70 (38 per cent) came from urban communities and 112 (61 per cent) from rural communities. Figure 2 shows the preponderance of rural cases from the South. This is attributable to the predominance of farming as an occupation in that area. In a random sample of 3000 soldiers, 68 per cent came from rural and 32 per cent from urban areas. Therefore, much to our surprise, more city men proportionately were found inept or otherwise inadequate for military duty. This finding is diametrically opposed to the one we described in an earlier paper.[3]

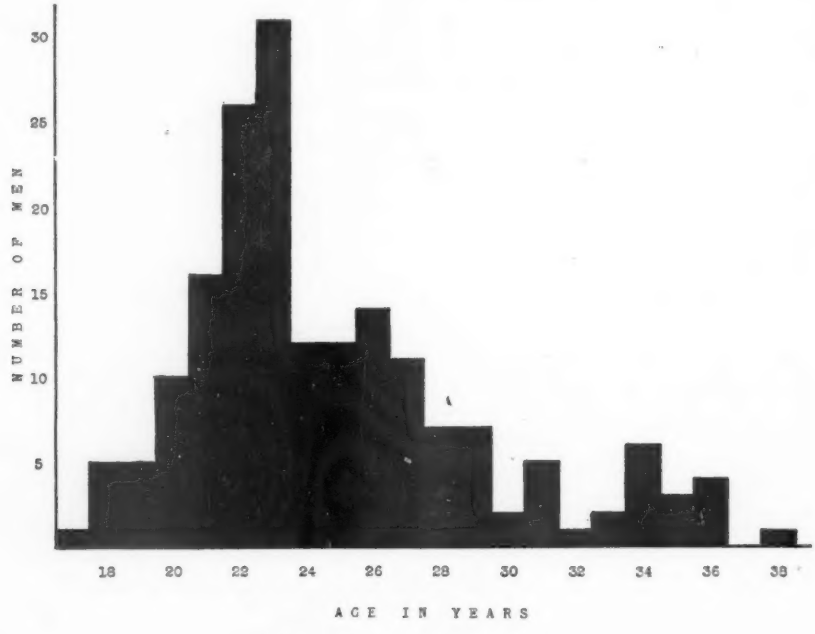

FIGURE 3. *Age at Discharge.*

AGE DISTRIBUTION

The age distribution of the men discharged (Fig. 3) was roughly parallel to that of the camp personnel as a whole. It demonstrates that inaptitude affects the same percentage of each group and that experience and increasing age do not enable the men to outgrow their difficulties. When the most frequent diagnoses, constitutional psychopathic state and mental deficiency, are considered this statement does not seem brash.

DISTRIBUTION BY TYPE OF MILITARY SERVICE

Of the 182 men discharged, 121 were infantrymen, 41 were from the field artillery, 8 were engineers, and 12 were from the hospital medical detachment. Exact percentages cannot be given, but it is certain that the smallest incidence occurred in the infantry, the next in the artillery, the next in the engineering corps, and the highest in the hospital detachment. This indicates that the more technical the work required, the greater the likelihood that inaptitude will be revealed. The large number from the hospital detachment is especially significant. Possibly working in the hospital educated these men in the ways and means of successfully simulating the constitutional psychopathic state. The incidence in this group was several hundred per cent higher than that to be expected in the other types of military service. This suggests that henceforth an additional check should be placed on those in similar positions.

DISTRIBUTION BY RANK

The distribution by rank (Table 2) was as follows: 170 men were privates, only 6 were noncommissioned officers, and only 6 were first-class privates. The extremely low proportion of first-class

TABLE 2. *Distribution by Rank.*

RANK	NO. OF MEN DISCHARGED	PERCENTAGE DISCHARGED	PERCENTAGE OF RANK IN THE ARMY
Private	170	93	52
Private, first class	6	3	30
Corporal	2	1	10
Sergeant	4	2	8
Total	182		

privates, corporals and sergeants to privates, in comparison with the ratio in the Army as a whole of one noncommissioned officer to every four privates, shows that most company commanders made promotions wisely.

Distribution by Occupation

Classification by occupation previous to military service (Table 3) was arbitrary. Each case was considered on its merits and given the full benefit of doubt; that is a higher rating was given whenever the question arose. Thus, store clerks were listed under "business," and truck drivers as "semi-skilled labor"; of the 4 men listed as "professional," two were students (exact status unknown), one was a Salvation Army fieldworker, and the last was a chiropractor. We admit that our generosity in rating is open to question; yet the occupational status of the series runs quite in accord with the expectation, the greater number of men being in the lower socioeconomic groups prior to induction.

Table 3. *Distribution by Occupation.*

Type of Occupation	No. of Men Discharged	Percentage Discharged	Percentage of Occupation in the Army*
Unskilled	105	58	28.7
Semi-skilled	32	18	23.1
Skilled	19	10	20.2
Business	12	7	18.4
Professional	4	2	9.6
Never employed	10	5	0

*Based on 3000 soldiers.

Diagnoses

Mental deficiency was the reason for discharge in 67 cases. The Kent E G Y test was used as a standard and was supplemented by other tests whenever indicated. The mental ages are shown in Table 4. Almost all these cases were said to show the "hypochondriasis of oligophrenia." Each presented multiple organic syndromes that required intensive investigation. Only when these had been disproved in the gastrointestinal, cardiac, urologic or other wards and much valuable time had thus been spent did they finally reach the neuropsychiatric section.

Table 4. *Mental Ages of Men Discharged for Mental Deficiency.*

Mental Age	No. of Men
Five years	1
Six years	2
Seven years	2
Eight years	15
Nine years	16
Ten years	19
Eleven years	8
Twelve years	4
Total	67

Two men were discharged with a diagnosis of neurasthenia gastrica. These diagnoses were probably erroneous, since it has been suggested by the Surgeon General's Office that such cases should receive a diagnosis of psychoneurosis, conversion hysteria. However, since these men were discharged under Section VIII they have been included in our series.

The rest of the men were discharged with a diagnosis of constitutional psychopathic state. This condition is classified by the *Standard Diagnosis Book* of the United States of America in seven groups: inadequate, paranoid, emotionally unstable, criminalistic, pathological liars, sexual psychopathy and unqualified. Of these, only three were used as the primary diagnosis: 55 men were listed as inadequate, 48 as emotionally unstable, and 19 as criminalistic. Occasionally, they were employed as secondary diagnoses.

In every case short but reasonably adequate histories were taken. So far as possible, childhood impressions, school records, former occupational situations, court and criminal records, sexual histories and personal relationships were probed.

Recommendations

We believe that each selectee and enlisted man, prior to his final induction into the Army, should be placed in a replacement center for a probationary period of three months. During this time a competent psychiatrist should assist the company commander in weeding out those psychically unfit for military duty before marked breakdowns occur or severe inadequacies make themselves apparent. The great majority of these cases, as well as most undetected psychoneurotic patients, could thus be eliminated without ever being actually inducted. This would save the Army the expense of many hospital days and spare the selectees the mortification of complete realization of failure.

Furthermore, this trial period should be served without prejudice to the Government, and barring physical disability incurred during it, the enlisted man or selectee should have no claim against the Veterans' Bureau. This arrangement would make possible the saving of both time and money. It would also aid materially in eliminating future compensation claims. It is impossible to estimate how many constitutionally psychopathic persons and mental defectives are now collecting government pensions because of a few months spent in an Army training camp in the last war. Judging from our experience, they spent even these few months in the hospital—their sole contribution then, as it is now—only to hinder the war effort.

SUMMARY

A report is given of 182 soldiers discharged from the Army through the Station Hospital at Camp Blanding, Florida, under Army regulations providing for the release of men who are incompetent or inept, or have habit or personality traits undesirable in a soldier.

The number of hospital days used, the time required for the recognition of inadequacy, and the distribution by geographical considerations, age, type of service, rank, civilian occupation and discharge diagnoses are discussed.

Some recommendations are offered to aid in the diminution of the number of these cases.

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4. Army Regulation 615-360, Section VIII.

MEDICAL PROGRESS

GYNECOLOGY: NEOPLASMS OF THE OVARY

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A REVIEW of the literature concerning ovarian growths shows that a large amount of information that is not generally possessed is now available. From the confusion of great numbers of ovarian cysts, cancers and benign tumors, considerable advance has been made in simplifying classifications and placing the various lesions in their proper niches. Robert Meyer[1-3] and Walter Schiller[4] have especially been in the vanguard for separating the special types from the enormous heterogeneous group of a few years ago. Many growths once considered malignant are now considered benign, and many tumors of more or less definite histology have been shown to be functioning tumors. Americans who have made special contributions to the subject of ovarian cancer and its treatment and prognosis include Lynch,[5] Geist,[6-10] Frank,[11-12] Taylor and Greeley[13] and Pemberton.[14] In this review it will not be possible to give credit to each investigator, but many important references are appended.

In a review of the literature it is perhaps not correct to present a classification of ovarian neoplasms, but the classification given below, based on Schiller's[15] recommendations, seems to simplify the whole problem.

CLASSIFICATION OF OVARIAN NEOPLASMS

It is obvious that the ovary must contain in itself many potential growth cells. It commences as a clump of mesenchymal cells on the posterior wall of the abdominal cavity behind the forming peritoneum. This primitive group of cells furnishes those that under certain circumstances become specialized cells, some of which may eventually be indistinguishable from epithelial cells. For instance, the primitive connective-tissue cells of the early gonad may surround an ovum and become granulosal cells or theca-interna or theca-externa cells. In contact with spermatozoa these same cells may differentiate into Sertoli cells or the supporting cells of the testicular tubule. Sometimes the cells that usually become differentiated do not change toward male or female cells, but remain neuter and develop into the cells of the disgerminoma or neuter tumor. The undifferentiated connective-tissue cells from which the differentiating cells arise form the stroma of the ovary, and from them may arise the fibroma and sarcoma of the ovary.

The epithelial covering of the ovary, arising as it does from the celomic epithelium of the pelvis, may differentiate into epithelial-like structures similar to those that arise from the celomic epithelium. As the celomic epithelium is the precursor of the müllerian ducts, it is easy to appreciate that epithelium similar to whatever the müllerian ducts might form may be present in the ovary. The upper vagina, the cervix, the endocervix and the endosalpinx are derived from these ducts. Therefore it is possible that squamous epithelium, endocervical epithelium, endometrial epithelium and endosalpingial epithelium may be present in certain tumors of the ovary. Schiller[15] has demonstrated that the pseudomucin noted in the so-called "pseudomucinous cysts" of the ovary is not pseudomucin but old changed mucin. Thus, if pseudomucin is mucin in certain mucinous cysts, it is probably

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derived from the cervical epithelium, such lesions being endocervical epithelial tumors. Simple cystadenomas, papillary cystadenomas, malignant papillary cystadenomas and solid cancers of all the above types therefore arise from the epithelium of the covering of the ovary. There is of course an unclassified group that may arise from a more primitive type of celomic cell.

Inasmuch as the primitive ovary grows in close proximity to the adrenal gland, the kidney and the primitive mesonephros and wolffian ducts, it is not surprising that tumors of these types are occasionally found in the fully formed ovary. Cells of organs arising near the ovary are incorporated in it during its growth and develop early or later in life. Thus the origin of the adrenal-cell tumor of the ovary and the mesonephroma and Brenner tumor is explained.

The ovary contains ova, and if one of these should be fertilized, either parthogenetically or otherwise, the ovary would probably contain tumors or cysts of cells from all other organs or tissues of the body. These growths when solid and made up of undifferentiated or differentiated cells are called teratomas, whereas the cystic types as a rule contain all three germ layers and are known as dermoid cysts. Thus the fertilization of an ovum in an ovary may produce tumors similar to the thyroid gland, cartilage, bone, the central nervous system, the intestinal tract or any part of the epithelial system. A tumor of intestinal epithelium in a dermoid cyst can easily explain certain other of the so-called "pseudomucinous tumors," which are really mucinous tumors. Pseudomucinous peritonitis arises from these tumors, but in both men and women it may be present in patients with mucoceles of the appendix. It is probable that the origin of such peritonitis is the mucus cells of the intestinal tract.

The ovary is also the seat of metastatic lesions. Tumors of the stomach metastasize to the ovary and are responsible for Krukenberg tumors, which are myxomatous in type and contain signet-ring cells that secrete mucus. Endometrial cancers of the uterus metastasize to the ovary, and these tumors cannot be differentiated from malignant epithelial tumors of the ovary formed from the primitive endometrial cells of the celomic epithelium. Thus there are two types of endometrial cancers of the ovary, one formed from the covering of the ovary and one metastasizing to it from the uterus. Other organs of the body may be responsible for metastatic tumors in the ovary — small intestine, bile duct, breast, large intestine, rectum and even the pigment cells of the eye.

Thus it is clear that neoplasms of the ovary may be grouped into those arising from the celomic epithelium covering the ovary, from the primitive mesenchymal cells, because of continuity and from fertilized ova and those metastasizing to it. The classification is as follows:

Tumors arising from celomic epithelium (vaginal, endocervical, endometrial, endosalpingial):
- Cystoma (endometrioma, endosalpingioma, adenoma, fibroadenoma)
- Papillary cystadenoma
- Malignant papillary cystadenoma
- Solid carcinoma

Tumors arising from primitive mesenchyme:
- Arrhenoblastoma
- Granulosal-cell, thecal-cell
- Luteoma, xanthofibroma theca cellulare
- Disgerminoma (neuter)
- Fibroma
- Sarcoma

Tumors arising because of continuity:
- Adrenal-cell
- Kidney-cell (hypernephroma)
- Mesonephroma
- Brenner (renal pelvis, ureter or urethra)

Tumors arising from fertilized ova:
- Teratoma, chorionepithelioma, struma
- Dermoid cyst

Metastatic tumors:
- From uterus (endometrial)
- From stomach (Krukenberg)
- From intestine (small or large), eye, rectum, breast, bile duct and so forth

These five sources include all the possible ovarian neoplasms, and such a grouping is not difficult to understand or remember. Physiologic cysts have been deliberately omitted because they are not true neoplasms but represent abortive ovarian function. Such cysts include atretic follicles, follicle cysts, corpus-luteum cysts and thecal-lutein cysts. These small cysts are important but should be considered in the abnormal physiology of the ovary and not among its neoplastic possibilities.

General Considerations

Careful and thorough investigations must be carried out in patients with ovarian tumors. Such investigations are those conducted in patients with abnormal bleeding, thyrotoxicosis, hirsutism, virilism, fluid in the abdomen and chest and increase or decrease in size of the breasts. One must be familiar with the technic of endometrial biopsy and peritoneoscopy. Laboratories must be available to determine the levels of follicle-stimulating hormone, estrin and pregnanediol, to measure the basal metabolic rate, to perform Aschheim–Zondek and Friedman tests and to determine the excretion of the androgens and 17-ketosteroids — the latter being a representation of adrenocortical function.

It must be remembered that at operation a pathologist should be present who can help to de-

termine the type of tumor with which one is dealing. It is essential in modern surgery to be able to distinguish benign from malignant tumors. Tumors that appear malignant in gross may be relatively benign; such is the disgerminoma, whose diagnosis is made more easily from a frozen section than from a fixed section. One should also be able to make a prognosis, based on the type of tumor found. Another reason for making a histologic diagnosis before the patient's abdomen is closed is to be certain that the tumor is not one that is likely to be bilateral, or to be of such a type that might metastasize to the uterine body and thence to the cervix. It is recognized that an occasional tumor will respond well to x-ray therapy: every gynecologist has had some patient who had metastases to the omentum or to the peritoneum, with fluid in the abdomen, and who, after removal of a certain amount of the primary tumor, responded to x-ray treatment, but these cases are rare.

The new syndrome[16, 17] of abdominal and chest fluid due to fibroma of the ovary must not be forgotten; if a patient has a tumor in the pelvis with fluid in the chest and abdomen, one must not conclude at once that the lesion is malignant. It has been shown that the removal of a simple fibroma of the ovary may cure such a condition. It is also true that cystadenomas and malignant papillary cystadenomas of the ovary may be accompanied by pleural as well as abdominal fluid. Reports have been made by MacFee[18] and Dannreuther[19] of such fluid in benign lesions, and by Schenck and Eis[20] in a malignant one. Recently a similar case was seen at the Pondville Hospital; the patient, who had a cancer of the ovary with fluid in the chest, was probably cured by removal of the ovarian tumor — there were no malignant cells in the centrifuged chest fluid.

Today, adequate knowledge demands that the surgeon recognizes the type of lesion, if possible, that he knows the proper investigative laboratory technics, and that he realizes how and when to use x-ray treatment. The last has never cured patients, but it has helped to make them live longer. It must be outlined by the roentgenologist in such a way that it is directed toward the tumor, toward the spilled portions of the tumor or toward the adhesions connected with the tumor. It is of no use for the surgeon to write a note to the x-ray department saying simply: "Carcinoma of the ovary. Please treat." This practice should be abandoned.

Tumors Arising from Celomic Epithelium

Cystomas of the ovary are true neoplasms and arise, as postulated, from the epithelium covering the ovary. They may be small or large; they may be single or multilocular; and they may contain serous or so-called pseudomucinous fluid. The epithelium may be of the tubal, endometrial or endosalpingial type, or even of an unclassified type. The possibility that this lesion is bilateral is great; therefore both ovaries should be examined carefully. This lesion is not malignant, and its simple removal from the ovary, if possible, or removal of the ovary itself with a careful inspection of the other ovary, is all that is necessary, but the patient must be watched.

Papillary cystadenomas present a different problem. These are potentially malignant. If the papillary growths are all on the inside of the ovary and if they are filmy and small and not infiltrating, the chances of their being benign are very great. However, they may be malignant microscopically. They are bilateral in 30 to 40 per cent of cases. One finds in these lesions the type of epithelium that grows from Müllerian epithelium — squamous epithelial, endocervical or mucinous, endometrial or endosalpingial. Proper treatment for the papillary cystadenoma is removal of both ovaries. However, because many of these occur in young women in whom the preservation of fertility is essential, one can be conservative but must watch carefully to make sure that there is no occurrence in the other ovary, which may be of the malignant type. If the pathologist finds an area that is suggestive of cancer, the responsibility of the surgeon is great. Should he reoperate and take out the other ovary? No one can solve this problem but the surgeon himself. Should he elect to reoperate and remove the other ovary, no one could criticize him.

A *malignant papillary cystadenoma* demands close scrutiny. If a papillary cyst of the ovary shows thickness of the wall, penetration through the wall of the cyst to the other side or papillary areas on the outside of the cyst, one must be very suspicious of malignancy. The pathologist cannot always assure the surgeon, but if the tumor is considered probably malignant, radical surgery should be carried out. By radical surgery is meant the removal of the uterus and the cervix, because the presence of metastases in the uterine wall means that there may be metastases in the cervix. The opposite ovary is involved in a large percentage of cases; therefore it also should be removed. The prognosis for these patients is about 21 per cent survival for five years — a very small percentage of curability. It must also be remembered that metastases from endometrial cancer are very similar to the endometrial type of malignant papillary cystadenoma. One must determine by curettage of the endometrium whether or not it is involved primarily and the ovary secondarily, or vice versa. Most surgeons believe that x-ray treatment is unnecessary if the lesion is removed in toto without spilling or with-

out evidence of adhesions. If spilling has occurred or if there are evidences of adhesions and of growth onto the bowel or peritoneum, x-ray treatment must be given; and, if so, the case must be discussed with the roentgenologist so that the x-rays can be directed in the proper direction.

Solid carcinoma of the ovary is the most serious of all the epithelial growths of this organ. The curability is very low, 9 per cent survival for five years. It is believed, however, that if the patient lives for two and a half years following removal of such a tumor, the chances of permanent cure are very great.[21] Patients with malignant papillary cystadenoma succumb more slowly than do those with solid cancers; if the solid cancers are cured, they are usually thoroughly cured. These tumors may be made up of the squamous-cell type of epithelium, representing the vagina, the mucinous, representing the endocervix, the endometrial, representing the endometrium, or the endosalpingial, representing the inside of the tubes; or they may be of an entirely unclassified type. Abnormal bleeding is not uncommon in these lesions. It is the general belief that the peritoneoscope is of great value in diagnosing this tumor, and it should be used frequently and without hesitation to determine whether the tumor can safely be removed or whether there are metastases throughout the abdomen. In spite of the fact that the abdomen and even the liver, or at least the surface of it, may be thus involved, one must consider removing the local growth, because for some reason or other this procedure may prevent rapid growth of these extensions. Metastatic areas and fluid have been known to vanish after removal of the primary growth; why, is not known. The question of dissecting lymph nodes in patients with solid cancer of the ovary is an important one. As yet this dissection cannot be advocated, but the time may come when, if more is known about where these metastases are likely to occur, removal of them will become part of the surgical approach. X-ray treatment should be given, as in malignant papillary cystadenoma, only when it is known where the tumor has extended.

Included in this group of celomic epithelial growths are the *endometriomas* and *endosalpingiomas* of the ovary and tube. These are benign lesions growing from the epithelium of the cortex down into the body of the ovary, forming the so-called "chocolate cysts." There is a difference of opinion whether these lesions come from the endometrium itself, the cells flowing through the tubes and alighting upon the ovary at the time of menstruation, or arise from the endosalpinx, attaching themselves to the ovary, or arise from the celomic epithelium covering the ovary. It is not unlikely that the last-named source is the primary one. These cysts grow to moderate size before they are so pressed on by connective tissue and ovarian capsule that function ceases. There is no question that the endometrioma menstruates, but how long it continues to do so is doubtful. Endometriosis of the pelvis, which may arise from an endometrioma of the ovary that has become adherent to the broad ligament or to the cul-de-sac, may be a serious lesion demanding radical surgery. However, most gynecologists believe that if one can be conservative one should excise the endometrioma from the ovaries or ligaments and save the pelvic organs so that future childbearing can take place. It is also believed that pelvic endometriosis is increasing, perhaps because of avoidance or postponement of pregnancy. Normal childbearing is most important in order to prevent the onset or growth of this lesion.[22]

Tumors Arising from Primitive Mesenchyme

The *arrhenoblastoma* is male-directed and is often, although not always, accompanied by virilism, masculinization, hirsutism and so forth. The testicular tubular adenoma of Pick is the most highly differentiated type. In patients showing physiologic effect of such a tumor the clitoris is enlarged, the scalp hair recedes, and the growth of hair increases in areas similar to those found in men; the breasts atrophy, the voice becomes deeper, and the patient assumes a mannish physique. Sometimes amenorrhea accompanies this tumor, but not always. The tumor may be small or large. It is usually freely movable and is not always malignant. It has been stated that removal causes the hair to recede, but it has been the experience of the Ovarian Dysfunction Clinic at the Massachusetts General Hospital that the hair does not recede but grows softer, without further increase. The voice rarely returns to normal, because there is an anatomic change in the larynx owing to the presence of this male tumor. The clitoris does decrease in size.

The diagnosis of this lesion in those in the menstruating age is not difficult because it so frequently causes amenorrhea and the above changes in the appearance of the patient. The follicle-stimulating hormone in the urine of such patients is extremely low, and the presence of a low titer of follicle-stimulating hormone, amenorrhea, hirsutism and the presence of an ovarian tumor indicate the diagnosis. Albright[23] thinks that a low titer of follicle-stimulating hormone is of extreme importance. The amount of 17-ketosteroids in the urine, which is primarily a measure of adrenocortical male hormone, is not necessarily disturbed; it may be high but usually is not. The arrhenoblastoma as a cause of symptoms should

be differentiated from Cushing's syndrome and adrenocortical hyperplasia, cancer or adenoma. In Cushing's syndrome the patient is not necessarily masculinized as in adrenocortical syndrome. Although in both these conditions the blood sugar metabolism is upset, the patient with Cushing's syndrome has osteoporosis, thin skin, hypertension, a protuberant abdomen, thin legs and arms and so forth, which may not be present in the patient with adrenal difficulty. The differentiation among these three is not easy, but if one has in addition an ovarian tumor, one should consider arrhenoblastoma first. Of arrhenoblastoma it has been said that the less differentiated the tumor, the more masculinized the patient. Miller,[24] quoting Meyer, says: "These are a group of tumors related from their morphological similarities, which, more often, and to a greater degree, cause masculinization the more the tumor differs from the testicle, that is, the more unripe it is. This appears contradictory but it is a fact." That has not been so in 4 patients seen at the Massachusetts General Hospital. Two patients with undifferentiated tumors had no masculinization and 2 of them (both with testicular tubular adenomas of Pick) had marked masculinization.

Arrhenoblastomas arise from cell rests derived from the primitive mesenchyme, whose cells after contact with spermatozoa are male-directed. The arrhenoblastomas are often tubular in form and most of them contain groups of Leydig cells, which secrete the male hormone. In Kanter and Klawans's case[25] (the microscopic slides were viewed by Schiller) there were areas of cartilage. This fact, plus the fact that in Krock and Wolferman's[26] case, when the tumor recurred, it contained cartilage, suggests that these tumors may be teratomas. In the very early stages they should have a histologic picture similar to that of the early granulosal-cell tumors, and this is true. It is difficult to distinguish an undifferentiated arrhenoblastoma from an undifferentiated granulosal-cell tumor.

The *granulosal-cell tumor* and the *thecal-cell tumor* should be grouped together. They arise from primitive connective-tissue cells that are directed toward the female after contact with ova; and very early growths, as stated above, are not distinguishable from early arrhenoblastomas. Granulosal-cell tumors grow in undifferentiated or differentiated form. In some there are evidences of attempts at follicle formation and ova may be thought to be present, but these have usually proved to be areas of degenerating cells, the so-called "Call–Exner bodies." No true ova are present in granulosal-cell tumors. Traut, Kuder and Cadden[27] suggest that these tumors arise in the granulosal cells of follicles, as Furth and Butterworth[28] showed, arising in x-ray treated mice. By properly staining (Foot silver stain) these tumors one can differentiate the thecal-cell and the granulosal-cell tumor or can observe a combination of both. The silver stain brings out the presence of reticulum or connective-tissue elements in the thecal-cell components.

These tumors are found in all ages of life. In youth they cause precocious femininity and menstruation, and in the age group following the menopause they bring about abnormal bleeding. Amenorrhea may accompany these tumors while the endometrium is hypertrophying, just as it does in metropathia hemorrhagica. Hyperplasia of the endometrium is common but not always found, but an estrin phase is always present. These tumors, through the estrin they produce, inhibit the pituitary gland and therefore prevent the formation of follicle-stimulating hormone in normal amounts. Removal of the granulosal-cell tumor after the menopause causes a cessation of abnormal bleeding, and hot flashes may ensue. Precocious bleeding and enlargement of the breasts may occur in children with this tumor; and removal of it causes a cessation of the bleeding and a return to normal. Not all precocious bleeding, however, is due to the granulosal-cell tumor, since it may be caused by such conditions as lesions of the hypothalamus and Albright's disease,[29, 30] with its brown spots and bone cysts. It must always be remembered that polyps, cancer and occasionally no lesion at all, may be found in women who have abnormal bleeding. Hyperplasia of the stroma of the cortex in the ovary or hyperplasia of the theca may be responsible for hyperplasia of the endometrium and bleeding in patients after the menopause.

Granulosal-cell tumors may be of any size, from very small to very large. They may be cystic but are usually solid. Their malignancy varies from 5 to 25 per cent. They have been reported as comprising as much as 10 per cent of all ovarian tumors, but this has not been the experience at the Massachusetts General Hospital. There are no absolutely diagnostic signs or symptoms, but abnormal bleeding or amenorrhea, the presence of hyperplasia of the endometrium and a tumor of the ovary in youth or old age are quite diagnostic, and the presence of persistent or estrin endometrium accompanied by a tumor of the ovary of solid type is also fairly characteristic. The presence of an adenofibroma of the breast in a woman past the menopause is very suggestive of an estrin-secreting tumor. Granulosal-cell tumors are commoner than arrhenoblastomas or disgerminomas, but they are not extremely frequent.

Under the heading of granulosal-cell tumor should be grouped the *luteoma* or luteinized granulosal-cell tumor and the *xanthofibroma theca*

cellulare or luteinized thecoma. These tumors are rare and are usually benign. They produce definite changes in the endometrium, causing a persistent secretory phase, and are often accompanied by marked decidual formation. Amenorrhea may be present. The presence of persistent secretory endometrium and periods of amenorrhea and bleeding when an ovarian tumor is present usually clinch the diagnosis.

The *disgerminoma* was formerly called a seminoma, as was the testicular tumor of the same histologic structure, but Meyer[31] showed that this tumor does not arise from the seminiferous tubules of the testicle, but rather has invaded them; therefore the old nomenclature had an incorrect basis and he called the growth "disgerminoma." *Dis* means "both"[15]; that is, the same type of neoplasm occurs in the male and the female. In the male it is considered extremely malignant, whereas in the female it is frequently benign. Seegar[32] says that the disgerminoma has a mortality of 35 to 60 per cent, basing his conclusion on 50 cases from the literature and on the results of treatment in 17 of 19 cases in his report. Of the 12 cases seen at the Massachusetts General Hospital, only 1 has proved to be malignant, and in that case the tumor had already begun to invade the surrounding tissue.

The disgerminoma is neuter; it arises from those primitive cells that might have developed into either granulosal or Sertoli cells but did not. It has no endocrine function. A large number of cases have been reported. The lesion can be recognized on frozen section as easily as from a fixed section. The tumor is made up of large round cells divided by connective-tissue-cell septa full of lymphocytes, and the presence of foreign-body giant cells is common. Disgerminomas were formerly called large round-cell carcinomas of the ovary; they were given x-ray treatment, and were frequently cured. The tumor is very radiosensitive, but it is also benign in the majority of cases, and therefore x-ray treatment should not be given, because some of the young patients might otherwise be able to have children. Many times the patient herself is a neutral, that is, her genital tract is not normally developed. In many of the cases at the Massachusetts General Hospital, however, there was normal female development. Moehlig[33] reports a case of intersexuality in a patient with malignant teratoma of the seminoma type. He was probably describing a disgerminoma, and possibly one that arose in an ovariotestis. Long et al.[34] report a disgerminoma in a pseudohermaphrodite. Among the cases at the Massachusetts General Hospital was that of a young girl of seven, with pubic hair, open vagina and a large clitoris. Pregnancy occurred in 3 patients following removal of the tumor. These tumors are supposed to be common in the ovariotestis. The ovario-testis itself is a rare lesion, not being a tumor but a physiologic abnormality, the gonads being made up of both ovary and testis.

Fibromas of the ovary arise from the nondifferentiating mesenchyme that is to become the stroma of the ovary. They are not uncommon. The size of the tumor varies from that of a small pea to that of an adult's head. It may grow on the outside of the ovary in papillary fashion or may include the whole ovary. Usually there is a firm capsule, and on section the tumor shows whirling areas of connective tissue as in uterine leiomyoma. It is well known that the condition is often accompanied by abdominal fluid. Recently Meigs and Cass[35] presented a number of patients with fibroma of the ovary with fluid in the chest as well as in the abdomen. Up to the present time 27 cases with fluid in the abdomen and chest have been reported in the literature.[16] The fluid may be in the right or left chest, or in both. The reason for its occurrence is unknown. Probably the fluid is formed in the abdomen and enters the chest cavity by way of the diaphragmatic lymphatics. This entity is important because patients who have an ovarian tumor with fluid in the chest and abdomen do not necessarily have a tumor that is malignant and has metastasized to the chest. Chest taps with centrifuging of the fluid and examination of the cells is extremely important, because if no malignant cells are present one may be dealing with a fibroma of the ovary, and its removal will stop formation of fluid in the chest as well as in the abdomen. Reports are already appearing in the literature of patients who were given up as hopeless but were relieved by surgical removal of the benign lesion. Ovarian cysts have been reported with the same findings, as have leiomyomas of the uterus. It must be remembered that ascites alone can occur with any large benign pelvic tumor.

Sarcoma of the ovary is rare and arises from the same primitive undifferentiated cells that form the stroma. Patients with true sarcoma do not do well and the prognosis is poor. If the diagnosis is made, removal of both ovaries is best. Removal of the uterus is not essential in these cases, since it is rare for metastases to occur there. Reclassification of sarcomas of the ovary in the laboratory has in many cases proved them to be other types of tumors.

Tumors Arising Because of Continuity

The *adrenocortical-cell* tumor is among the group arising from continuity. Inasmuch as this part of the adrenal gland contains a male-directed hormone, such a tumor in the ovary may produce

masculinization, hirsutism and so forth, just as may an adrenocortical cancer, tumor of hyperplasia. Novak[36] has recently reported 3 patients with adrenal-cell tumors of the ovary with masculinization. Clear-cell tumors of the ovary, so often considered as adrenal, are not necessarily of the masculinizing type, nor are they necessarily adrenal. They may be clear-cell carcinoma of the kidney, the *hypernephroma.* This tumor is not accompanied by any definite symptoms. Van Kirk and Edwards[37] describe a hypernephroma of the ovary. A patient with a functioning adrenal-cell tumor of the ovary may become masculinized with male configuration, hair, large clitoris, change in voice, amenorrhea and so forth. There may or may not be a change in the sugar metabolism, but one would certainly expect it. There should be an increase in the excretion of 17-ketosteroids. The presence of an ovarian tumor accompanied by the above symptoms should be investigated by all available laboratory methods, and differentiation from an arrhenoblastoma is difficult unless the 17-ketosteroids and the sugar curve are estimated. If the 17-ketosteroids and sugar metabolism are upset, the adrenal glands should be explored by air injection and an intravenous pyelogram. If nothing abnormal is found, surgery should be undertaken, and there are definite possibilities of finding an active adrenal tumor.

The *mesonephroma,* which Schiller[38] has described, contains primitive glomeruli and probably arises from the primitive kidney or mesonephros. It occurs in the ovary because of the closeness of the mesonephros to the primitive gonad. These tumors are probably benign, and conservative treatment is usually the method of choice; however, Rosenblatt and Grayzel[39] have recently recorded a malignant mesonephroma.

Tumors of the *Brenner* type probably arise from the type of epithelium that is present in the kidney pelvis, ureter and urethral orifice.[40] Small clumps of stratified transitional epithelium are found in areas in the ovary, which has the appearance of a fibroma. Novak and Jones[41] believe that Brenner tumors arise in the Walthard islands of indifferent cells in the ovary, and that the epithelium cells of the Brenner tumor may develop into pseudomucinous cells and later form pseudomucinous cysts. The Brenner tumor is found along with the so-called "pseudomucinous cystadenoma," and it is possible that this lesion might arise from a teratomatous development. The epithelium, however, is probably representative of the epithelium of the urinary tract.

Tumors Arising from Fertilized Ova

The fertilized ovum in the ovary may produce any sort of tumor or cyst. The ovum is considered as fertilized parthenogenetically, or the teratoma may be considered as a twin of the host. Fertilization occurs in some manner that we cannot explain. Shaw[42] does not believe in the parthenogenetic theory but thinks that teratomas may arise from some functioning sex cell. He supports his belief by stating that most teratomas are formed of adult cells; if they were to arise from a fertilized ovum there should be a trophoblast, but there is none. He concludes that he does not know the origin of these tumors.

The *teratoma* is usually solid, composed of one type of tissue, such as thyroid, nerve tissue, cartilage and so forth, although Smeltzer[43] reports a solid malignant teratoma with three germ layers. The cells may be primitive and unrecognizable as being of any particular type, and in some cases are so undifferentiated as to be called embryonal. This represents the most primitive type of teratoma. Teratomas may or may not be malignant. They may invade and metastasize. If definitely malignant, radical surgery should be undertaken, with removal of the other ovary, the uterus and the cervix. If the malignancy is doubtful, radical surgery is still the best procedure.

Dermoid cysts are highly differentiated types of teratomas made up of two or three of the germ layers and often containing nerve tissue, skin, hair, teeth, bone, cartilage and so forth. Some of these lesions are malignant; most are benign. It is possible for a dermoid cyst to show malignant-looking areas and yet be a benign lesion. This picture is similar to what one sees in the parotid-gland mixed tumors, where there may be the most active-appearing carcinoma, and yet if any cartilage is found in the same tumor it is usually a locally malignant lesion only. Such a tumor will recur, but will not metastasize. Dermoid cysts with malignant areas act in the same way; that is, they may be malignant in appearance only, but they can be and sometimes are extremely malignant. The usual treatment of the simple dermoid cyst is excision with the ovary or excision from the ovary. About 8 per cent of these cysts are bilateral.

Chorionepithelioma of the ovary must be considered as a teratoma. Simard[44] has recently seen 2 cases of chorionepithelioma and believes in its parthenogenetic origin. Such a lesion would of course give a positive Aschheim–Zondek test, being composed of chorionic tissue. The chorionepithelioma is occasionally extremely malignant.

In the teratoma group there may be pseudomucinous cystadenomas arising from epithelium similar to the epithelium of the small intestine. Such a tumor is similar in appearance to the pseudomucinous cystadenoma of the endocervical type described above. The presence of hair or cartilage in such a cyst places it in the teratoma group.

Otken[45] has recently reported a primary mel-

anotic sarcoma of the ovary. This rare lesion is probably of teratomatous origin.

Struma or thyroid tumors of the ovary are not very rare and may include the whole tumor or a small area in a cystic growth. The thyroid tissue appears to be normal, and its iodine content is the same as that of normally placed thyroid tissue. Emge[46] believes that 5 per cent of these tumors are toxic, and he reports a typical case. He quotes other authors with apparent authoritative cases. These tumors are usually benign but may be malignant.

Metastatic Tumors

The commonest metastatic tumor of the ovary is that due to the metastasis of *endometrial cancer*. There is often difficulty in recognizing whether this metastasis has occurred, or whether the endometrial type of cancer in the ovary is primary there, growing from the celomic epithelium. It is important, therefore, to curette patients with ovarian cancer in order to be sure that there is no cancer in the endometrial cavity. It has been the experience of most surgeons that involvement of the ovary from endometrial cancer indicates a very bad prognosis.

The *Krukenberg tumor* of the ovary, a metastatic tumor, is usually bilateral and smooth and has a thick capsule. On section it is myxomatous and suggests sarcoma. There is considerable controversy whether or not there is such a thing as a primary Krukenberg tumor of the ovary; there may be, but such a lesion should be considered a teratoma. Certainly the usual tumor is metastatic, the primary tumor being in the stomach. They arrive in the ovary by way of the retroperitoneal lymphatics and the lymphatics of the mesosalpinx, meso-ovarium, uterine wall and tube, and are usually full of cancer cells. The gastric-cancer cells do not float down to the pelvis, alight upon the ovary and then grow. This type of growth is not papillary on the outside of an ovary but is smooth and symmetrical and has obviously grown from the inside of the gonad.

Tumors of the small intestine metastasize to the ovary, and although similar in gross to Krukenberg tumors are frequently adenocarcinomas. Those metastasizing from the large bowel and rectum are of the same type as the primary ones; they are usually unilateral. In patients with widespread lesions of the breast or of the bile ducts, involvement of the ovary is not uncommon, but it is rare to find a tumor of the real Krukenberg type, that is, bilateral, large, smooth tumors. The metastasis of breast cancer to the ovary is usually a terminal finding. If, at operation, tumors of the ovary are found that are bilateral, smooth and kidney shaped, a primary source in the stomach or intestine must be searched for. There are tumors from other sources that may metastasize to the ovary, such as melanoma of the eye, cancer of the cervix or tube and so forth.

Summary

This discussion of ovarian tumors demonstrates that more tumors have been grouped together and that a simpler classification is possible. Many tumors of highly specialized types have been removed from the large group of ovarian tumors and more appropriately reclassified. Functioning or endocrine tumors have been recognized.

The treatment of certain ovarian lesions is definite and may be conservative, but the proper treatment of malignant ovarian epithelial growths is by means of radical surgery, with removal of both tubes, both ovaries, the uterus and the cervix. It is important to recognize that the other ovary should be removed in malignant papillary cystadenoma or solid cancer because of the large percentage of these tumors that are bilateral, and that the uterus and cervix should be removed because of the possibility of metastases into the uterus and thence into the cervix.

It has been demonstrated that x-ray treatment is not too successful and must never be allowed to influence the surgeon as against radical surgery. Roentgen-ray treatment will prolong life but will not cure the patient. It has been obvious in all clinics that the x-ray treatment given in the past has not necessarily been given over the area of the extension of the growth. It is extremely important that the roentgenologist be shown by the surgeon where the tumor has been left behind or spilled so that the x-rays can be properly directed.

Knowledge of the pathology and histology of these tumors is of great importance. The presence of a pathologist at the operation is essential, for an expert can often differentiate one type from another. Thus the pathologist can help in the decision of whether or not to be radical.

If a mistake has been made and an ovary left in that might be involved, either because the tumor is often bilateral or because of the chances of a metastatic lesion, it is better to reoperate than to risk x-ray treatment. X-ray treatment should not be used to replace radical surgery.

Ovarian tumors are now receiving the attention of the endocrinologist and the medical man as well as the surgeon and the pathologist, which is well. The presence of functioning tumors of endocrine type has greatly increased the interest in all ovarian tumors. Special tests and special methods of investigation are now undertaken in patients who have abnormal physiologic responses possibly due to a tumor of the ovary.

Early recognition of ovarian tumors through careful history-taking and careful physical examination is possible, and operation on suspected ovarian tumors should never be delayed. The peritoneoscope should aid greatly in making the diagnosis in any suspected case. Early diagnosis is most important of all.

264 Beacon Street

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTE-MORTEM AND POST-MORTEM RECORDS AS USED IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

CASE 29021

PRESENTATION OF CASE

A sixty-five-year-old retired farmer entered the hospital complaining of cough with blood streaking of the sputum and chest pain.

The patient had been well until nine months before admission when he developed mild left midchest pain, which was aggravated by breathing. He ascribed the pain to his "heart" and rested in bed for two weeks. Although he still did not feel up to par he became ambulant. Three months later, that is, about six months before admission, he began to cough and raise some whitish sputum. He also developed pleuritic pain in the left lower chest and back. Soon the cough grew worse and the sputum, although not foul, became constantly blood streaked. He finally consulted his physician, who strapped his chest and had an x-ray taken, which showed an "abscess of the lung." On occasions he felt feverish, but there was no history of chills, night sweats, hoarseness or dyspnea. He lost about 25 pounds in the course of this illness. At the time of admission he was raising about a cupful of sputum daily. There was no history of an antecedent upper respiratory infection or operation. Several samples of sputum had been reported negative for tubercle bacilli.

The patient had had pneumonia five years before entry. The family history was irrelevant.

Physical examination revealed a gaunt elderly man who showed evidence of recent weight loss. He had a frequent hacking cough productive of a small amount of blood-stained mucus and complained of pain in the back and left chest. The chest was long and barrel shaped and moved very little with respiration. In the left back between the scapula and spine there were tenderness, dullness, decreased bronchovesicular breathing and tactile fremitus and normal whisper and vocal fremitus. The rest of the lungs seemed well aerated and emphysematous. There was a faint apical systolic murmur, and a loud blowing aortic systolic murmur. Examination of the abdomen was negative. There were a few small, firm, rounded, movable nodes in each axilla.

The blood pressure was 104 systolic, 62 diastolic. The temperature was 98.6°F., the pulse 88, and the respirations 28.

Examination of the urine was negative. The blood showed 12.6 gm. of hemoglobin and a white-cell count of 10,200, with 88 per cent polymorphonuclears. The sputum was negative for tubercle bacilli. A blood Hinton test was negative.

Roentgenograms of the chest showed, in the apex of the left lower lobe, a thin-walled cavity, 8 cm. in diameter, with relatively little surrounding reaction; it contained fluid and air. The remainder of the lung field was bright, except for scarring at the right apex; numerous blebs were visible. The diaphragm was low on both sides and showed limited expiratory motion. There was a small amount of fluid in the left costophrenic angle. The ascending aorta was dilated and calcified.

A sputum culture yielded a moderate growth of beta-hemolytic streptococci, and on the seventh day the patient was started on sulfadiazine, 5 gm. daily. On the eleventh day the white-cell count was 16,600. After ten days of chemotherapy another chest roentgenogram showed relatively little change.

An operation was performed on the eighteenth day.

DIFFERENTIAL DIAGNOSIS

DR. LOWREY F. DAVENPORT: We have here a constantly recurring diagnostic problem. There is sufficient information on which to base a diagnosis of lung abscess. There are two questions to be answered. Is this a simple abscess or an abscess secondary to tumor? And, in either case, what is the indicated treatment?

We can reasonably exclude tuberculosis on the basis of several negative sputum examinations, the age of the patient and the location of the lesion. Although the x-ray films showed old apical tuberculosis on the right there is nothing to indicate that this process had been reactivated.

The differential diagnosis lies then between simple abscess and one secondary to tumor. What evidence do we have from the symptoms? In a case of this sort the symptoms may be misleading. Often with proved cancer, the principal symptoms are those of infection beyond the growth. Such cases, then, give presenting complaints of an inflammatory process, and the possibility of tumor may be overlooked. Productive cough, sputum, pleural pain and fever are common to both conditions. Two complaints, however, stand out here. The sputum is recorded as being constantly blood streaked. This in my experience almost invariably

means cancer. Tuberculosis, bronchiectasis and lung abscess may cause streaked sputum intermittently. A constantly bleeding process is usually due to a growing and friable tumor.

The complaint of chest pain favors cancer. Although an abscess with pleural inflammation gives pain, it is rarely so constant and severe as indicated here.

At this point, on the basis of history alone, I should make a presumptive diagnosis of cancer. What additional evidence must we examine?

The age of the patient favors cancer. His sex gives at least a four-to-one chance in favor of the diagnosis.

Physical examination only confirms what we suspect. The chest signs are consistent with an inflammatory process in the left lower lobe. The absence of a wheeze is not necessarily disturbing. A persistent wheeze always means a bronchial obstruction, but wheeze may be absent in varying degrees of blockage. Palpable axillary nodes in an elderly emaciated patient can be given no weight.

The laboratory was noncommittal. There was a mild degree of anemia, and a slight leukocytosis. Negative but weighty evidence is given by the sputum reports, on the basis of which I have excluded tuberculosis.

May we have the x-ray films?

Dr. James R. Lingley: Here is the cavity described lying in the middle of the left lung field. Its walls are thin and smooth, and there is a well-defined fluid level in its upper third. In the lateral view, the cavity is seen to lie posteriorly and to occupy the apex of the lower lobe. A Bucky film shows no evidence of rib or spine involvement, the bones appearing normal except for generalized decalcification. The lungs also show emphysema and an old tuberculous infection of the right upper lobe, which is probably healed. The left costophrenic angle is obliterated by a small amount of fluid or thickened pleura.

The heart is small, and the aorta shows marked tortuosity, with definite dilatation of its ascending and arch portions.

Dr. Davenport: The roentgenograms show only a large abscess. There is no demonstrable tumor mass or sign of bony metastasis. This evidence is equivocal, as neither is necessary to sustain a diagnosis of bronchial cancer.

Summing up the findings then, we have a sixty-five-year-old man complaining of cough, persistent chest pain and constantly streaked sputum, with a demonstrable abscess and a sputum negative for tubercle bacilli. My working diagnosis on these findings is bronchial cancer with secondary abscess.

What treatment are we justified in offering such a man? If we are correct, he is doomed to a progressive and painful course terminating in death. An exploratory operation is certainly justified. Suppose we are wrong, what weight should we give that possibility? The outlook for cure in an abscess of such size and duration is uniformly poor. Dr. Richard H. Sweet* has found no case of spontaneous cure in such abscesses with a duration greater than six months. Our patient is still faced with a slower, less painful, but progressive process, which untreated may eventually cause death.

Knowing the outlook with less bold measures in either case, I should accept the risks of exploratory operation. Further decisions must await the findings at the time of operation. Drainage would be palliative only. With an irreparably damaged lower lobe, its removal, whether for abscess or cancer, offers the only hope of permanent cure.

Dr. Eugene R. Sullivan: Dr. King, you saw this case. Would you care to comment?

Dr. Donald S. King: I saw this patient in consultation, and I know what was found at operation, so that I can hardly approach the problem of diagnosis with an open mind. I do, however, wish to give hearty support to Dr. Davenport's insistence that bloody sputum over a long period almost always comes from carcinoma. This is particularly true if there is bloody mucus rather than blood mixed with pus. In retrospect the diagnosis in this case seems almost established by the persistent bloody expectoration, with obvious weight loss and chest pain.

When I first saw the patient I advised against bronchoscopy or operation and suggested a trial of chemotherapy. Former experience, however, had given us little hope that sulfadiazine would have a favorable effect on such a chronic abscess.

I wonder whether bronchoscopy would have given a diagnosis and whether it would have helped in the handling of the case. Dr. McGahey helped in the operation, and I should like to have his opinion whether the process was so located that it could have been seen through the bronchoscope.

Dr. Claud E. McGahey: I believe it was so located. However, I am against the routine use of bronchoscopy in persons of this age group.

Dr. King: I think that I advised against bronchoscopy for two reasons: first, because of the patient's general condition and, second, because of the lack of clinical or x-ray evidence of bronchial obstruction, either partial or complete. I do not, however, have a dread of bronchoscopy if prop-

*Sweet, R. H. Lung abscess: an analysis of the Massachusetts General Hospital cases from 1933 through 1937. *Surg., Gynec. & Obst.* 70:1011-1021, 1940.

erly performed, and I should like Dr. Davenport's opinion concerning the risk in this case.

DR. DAVENPORT: I should not favor bronchoscopy here. We have rarely found a cancer in the range of bronchoscopic biopsy where there has been no wheeze or x-ray evidence of obstruction. Secondly, as I see the situation, I am committed to an exploration with or without a preliminary biopsy, and the results of bronchoscopy would not change the plan of treatment. A factor in a borderline case is the slight but admitted risk of bronchoscopy in a man showing x-ray evidence of a dilated and probably eggshell-brittle aorta. I should accept this risk if I felt bronchoscopy might give evidence that would dictate the plan of treatment.

CLINICAL DIAGNOSES

Abscess of lung.
Bronchiogenic carcinoma?

DR. DAVENPORT'S DIAGNOSES

Bronchiogenic carcinoma.
Secondary abscess.

ANATOMICAL DIAGNOSES

Epidermoid carcinoma (Grade II), bronchiogenic.
Abscess of lung.

PATHOLOGICAL DISCUSSION

DR. SULLIVAN: Dr. McGahey, you participated in the operation. Will you tell us your findings?

DR. MCGAHEY: I had the opportunity to follow this case with Dr. Churchill, who subsequently operated on the patient. Efforts to establish a definite diagnosis did not include bronchoscopy because we thought that the procedure was too risky in a man of this age with a dilated and rigid aorta.

We questioned the benefits to be gained from external drainage but concluded that if we could minimize the cough by such a procedure the patient might be made temporarily more comfortable. The operation was thus undertaken primarily with palliation in mind and secondarily to establish a diagnosis that, in the event of malignant disease, would justify x-ray therapy later.

The seventh intercostal space was exposed over the left paravertebral area. The intercostal muscles were found to be moderately edematous. Needle aspiration recovered a few cubic centimeters of moderately thick nonfoul pus from a point about 5 cm. deep to the eighth rib. A segment of the eighth rib was resected, and the subjacent tissue was found to be firm and rubbery, and grated under the cut of the knife. A biopsy specimen was taken. The cavity was then opened through this tissue and found to contain about 40 cc. of nonfoul pus. Tube drainage was established.

Convalescence was uneventful. The cough was considerably lessened, but when discharged the patient was still having moderate discomfort in the wound.

DR. SULLIVAN: Microscopic examination of the material removed at operation showed an epidermoid carcinoma of comparatively low-grade malignancy. It is therefore evident that the abscess was secondary to the neoplasm, as Dr. Davenport predicted.

DR. KING: Was lobectomy considered?

DR. MCGAHEY: The growth had extended through the pleura at the site of drainage. In any event this man would not have been a reasonable lobectomy risk.

CASE 29022

PRESENTATION OF CASE

A thirty-three-year-old housewife entered the hospital complaining of frequency, nocturia and incontinence of one year's duration.

The patient's husband had been injured in an automobile accident fourteen months previously, and since then she had been very nervous. One year before admission she developed urinary frequency and slight nocturia, and on several occasions during sleep she had total incontinence. Urinary incontinence was very frequent during any emotional disturbance. There was no dysuria, chills, fever or weight loss, but the patient had noted tremor, sweating and emotional instability. For the two weeks prior to entry she had had five or six bowel movements daily and also mild epigastric distress after meals. There were no menstrual abnormalities.

She had had thyroid enlargement for a number of years and had been treated until ten years before entry. She had had a mild "nervous diarrhea" for three months, five years previously. She had five children, all born at home; no perineal repair had been performed.

Physical examination revealed a well-developed and well-nourished woman with warm moist skin, moderate flushing and dermographia. The eyes were normal. The thyroid gland was slightly enlarged. Examination of the heart and lungs was negative. The abdomen was flat and soft. In the right lower quadrant was a nontender movable mass measuring 4 by 1 cm. Pelvic examination showed a slight rectocele and cystocele and a little prolapse of the urethra. No incontinence was demonstrated. The cervix contained a few nabothian cysts. The fundus of the uterus was not enlarged and was in normal position.

There was some tenderness in the right vault, but no masses were felt. Rectal examination confirmed the pelvic findings.

The blood pressure was 145 systolic, 100 diastolic. The temperature, pulse and respirations were normal.

Examination of the urine was negative. The blood showed a white-cell count of 13,000 and 15 gm. of hemoglobin. The basal metabolic rate was +7 per cent. A blood Hinton test was negative.

A barium enema showed a normal colon. There was retrograde filling of the terminal ileum, which appeared normal. The appendix was not visualized, but there was a small pressure defect at the lower pole of the cecum.

An operation was performed on the fifth hospital day.

Differential Diagnosis

Dr. S. Peter Sarris: One is first impressed by the lack of help afforded by the story of frequency, nocturia and incontinence in a thirty-three-year-old mother of five children. Usually, the chief complaint not only offers a fairly good clue to the diagnosis but also allows for a little mental sport in a preliminary or snap diagnosis.

It is a wise rule that one should never be satisfied to treat something incidental to the patient's chief complaint until a satisfactory explanation for the latter has been found. The promising lead of incontinence fades completely away as one reads further that on physical examination "no incontinence was demonstrated."

Dr. John B. McKittrick: The abstract is misleading since incontinence was frequently demonstrated subsequent to the first physical examination.

Dr. Sarris: We are told "the urine was negative." I assume that more than one examination was done, and that there existed evidence of good urinary function as shown by good concentration.

Dr. McKittrick: Numerous urine examinations were done and were negative.

Dr. Sarris: Under such circumstances frequency and nocturia usually mean local pelvic derangement associated with previous childbirth.

There is no evidence of other factors, such as a mass pressing on the bladder and an irritative process in close approximation to it. Urinary incontinence that is "occasionally total" during the night and only on emotional disturbance during the day is usually on a psychic basis. A patient with a small vesicovaginal fistula may be continent during the day because of frequent emptying of the bladder but incontinent during the night when the bladder is allowed to fill more. Such a fistula, however, would not explain the emotional incontinence. One could discuss at great length the diagnostic possibilities of this patient's urinary complaints. However, I shall limit the discussion, since I do not believe that her complaint was significant so far as the main diagnosis was concerned.

As I see it, the important thing is the tumor in the right lower quadrant of the abdomen. With urinary complaints such a tumor would first suggest an ectopic atrophic kidney. Fortunately, however, the x-ray localizes the mass at the lower border of the cecum. This plus the pelvic examination also excludes a lesion of the uterus and adnexa.

We are told that she had had five to six bowel movements a day for two weeks. There is no description of these bowel movements regarding fluidity, mucus, pus, amebas or blood, either before or after entry. Also, there is no elaboration of the story of "nervous diarrhea" five years previously. Without all this information one is seriously handicapped in narrowing down the field of diagnostic possibilities.

May we see the x-ray films?

Dr. James R. Lingley: This defect involving the medial margin of the tip of the cecum is very small (Fig. 1). There is slight filling of the orifice of the appendix, which is seen to lie in the center of the defect. The terminal ileum is well filled and appears normal except for a few fine serrations on its lateral margin, which are probably due to spasm where the ileum is in contact with the mass. The mucosa appears entirely normal on the post-evacuation film. The defect in the medial margin of the cecum is still present after evacuation of the enema, in spite of the fact that the cecum has changed its position, showing that the mass is probably adherent to the cecum. I therefore interpret the films as showing a mass in the position of the appendix that produces a small pressure defect in the cecum.

Dr. Sarris: Do these small serrations in the film mean mucosal ulceration?

Dr. Lingley: The mucosa in both the cecum and the terminal ileum appears normal.

Dr. James H. Townsend: Were pyelograms done?

Dr. Lingley: No.

Dr. Sarris: Tuberculosis should be considered, but there does not seem to have been sufficient gastrointestinal disturbance. There was no fever, no weight loss, and no evidence of tuberculosis elsewhere.

Hypertrophic amebiasis can present in this way, but I cannot make the diagnosis without a history of amebic dysentery or of amebas in the stool.

Carcinoma can be fairly well excluded, chiefly on the basis of lack of mucosal involvement.

Lipomas and leiomyomas occur in this area in the wall of the cecum. They are both rare. I do not ever hope to make a preoperative diagnosis of either.

Large lymph nodes about the ileocecal valve, as part of a lymphomatous process or tuberculosis, could give a palpable mass indenting the cecum. However, these diagnoses could be made only by inference from evidence of either disease elsewhere in the body.

Regional enteritis sometimes starts in this way and produces a similar mass. However, there are usually more gastrointestinal symptoms than are recorded, and some pain. Moreover, the mass is often tender, at least slightly. There are ordinarily some fever and weight loss. The x-ray films are interpreted as showing only a pressure defect on the cecum and spasm of the ileum without sign of ulceration. In the face of the foregoing evidence I cannot make a diagnosis of regional ileitis.

Acute appendicitis is so frequent that very atypical forms of it are as common as any of the rare lesions of this area. However, in the absence of any history of pain and tenderness, I cannot make that diagnosis. Still I would not be greatly surprised if this were a subsiding acute appendicitis.

Mucocele of the appendix should be considered. A true mucocele of the appendix is rare. They are usually larger than this and likely to give more local symptoms. In some cases there exists an antecedent history of appendicitis. A certain number of cases are believed to follow a ruptured appendix, with subsequent resolution and formation of a cystic cavity containing mucus. Wangensteen* has produced mucoceles in animals in this manner.

Finally, carcinoids are rare, but the appendix is by far the commonest site in the gastrointestinal tract for this tumor. They may be locally recurrent or metastasize to the regional lymph nodes. They give mild irritative or obstructive symptoms

A B

FIGURE 1. *X-ray Films before* (A) *and after* (B) *Evacuation of a Barium Enema. The arrows point to the minimal swelling of the mucosa of the terminal ileum.*

*Wangensteen, O. H., and Dennis, C. Experimental proof of the obstructive origin of appendicitis in man. *Ann. Surg.* 101:629-647, 1939.

as they progress. They occur at practically any age but most commonly in the thirties.

Before concluding, there remains one more aspect to be explained. The patient is described as having emotional instability, tremor and sweating. I cannot readily explain these symptoms, and I do not know how definite they were. Perhaps she was just a nervous housewife. They could represent residual hyperthyroidism. There is mention of some kind of thyroid trouble ten years previously. But the essentially normal basal metabolic rate, the normal pulse and the lack of cardiac enlargement after all these years are against it.

One might conceive of a remote interrelation of the nervous symptoms, the hypertension and the right-lower-quadrant mass. Carcinoid tumors are argentaffinomas and developmentally related to adrenal medullary tumors, which have been described as causing paroxysmal hypertension. But carcinoids are nonfunctioning tumors, so far as I know.

In summary, I attribute the urinary symptoms to post-partum damage of the pelvic floor. The emotional symptomatology and tremor can be assigned to a psychic origin. In the absence of more gastrointestinal data and on the basis of a small nontender movable mass indenting the lower part of the cecum, I hazard the diagnosis of carcinoid of the appendix.

DR. EUGENE R. SULLIVAN: Dr. Bartlett, you saw this case. Will you add to the discussion?

DR. MARSHALL K. BARTLETT: As stated in the history and as emphasized by Dr. Sarris, this patient's presenting complaint was urinary incontinence. The story was much more definitely one of straight exertional incontinence than is given in the summary, and we were satisfied that it was explainable on the basis of the trauma of repeated childbirth.

The finding of a mass in the right lower quadrant was entirely incidental, but once it was found it was obvious that its nature must be investigated and explained before dealing with the chief complaint.

In evaluating this patient before operation, our line of reasoning followed much the same pattern as that outlined by Dr. Sarris. We excluded a tumor of pelvic origin on the basis of the physical examination, and ruled out an intrinsic lesion of the cecum or terminal ileum by virtue of the x-ray findings. Some process involving the appendix seemed the best explanation for the constant pressure defect of the cecum, and we believed that either a mucocele or a carcinoid would be found.

DR. SULLIVAN: Dr. McKittrick, will you tell us about the operative findings?

DR. MCKITTRICK: We operated on this patient thinking she had a tumor of the appendix, possibly a mucocele or a carcinoid. The barium enema had shown a pressure defect of the cecum (extrinsic), and the fluoroscopist was satisfied that the terminal ileum was normal. However, the terminal ileum proved to be the site of an early but well-established and typical regional enteritis. The bowel wall was uniformly thickened, slightly pale and less pliant than normal. The lacteals were prominent. Enlarged soft lymph nodes were scattered throughout the entire small-bowel mesentery. The process extended 25 or 30 cm. proximal to the ileocecal valve, gradually shading off to normal small intestine about 45 cm. from the cecum. The latter was a little thickened and injected. We were faced with the problem of what to do about this serious situation. The patient presented none of the usual requisites for surgery, namely, obstruction or fistulas. In fact she had been bothered by her disease only on two short occasions. Experience with early cases of regional ileitis has produced equivocal data regarding the benefits to be gained from early surgery. However, this seemed an ideal case to benefit from surgery if the adherents of early radical excision are correct. An end-to-side ileo-transverse colostomy was done as the first stage of a two-stage right colectomy. During the subsequent operation, all the grossly involved ileum and as much of the mesentery as could be obtained were removed. Still later, a urethroplasty was done to cure the urinary incontinence.

DR. GRANTLEY W. TAYLOR: What was done with the distal bowel?

DR. MCKITTRICK: The open end was turned in.

CLINICAL DIAGNOSES

Mucocele of appendix?
Carcinoid of appendix?
Urinary incontinence, due to urethrocele.

DR. SARRIS'S DIAGNOSES

Carcinoid of appendix.
Relaxed pelvic floor, with incontinence.

ANATOMICAL DIAGNOSES

Regional ileitis, acute, active.
Normal appendix.

PATHOLOGICAL DISCUSSION

DR. EUGENE R. SULLIVAN: The last 25 cm. of terminal ileum showed a thickened wall with an edematous mucosa. Just proximal to the ileocecal valve the edema was more marked and accom-

panied by a few shallow mucosal ulcerations. The largest of these measured 1.0 by 0.3 cm. The attached mesentery of the small bowel contained many soft lymph nodes. Microscopically these showed no resemblance to the picture seen in sarcoid. The appendix was completely normal.

DR. MCKITTRICK: Would a small-bowel series have revealed a clue to the true diagnosis?

DR. LINGLEY: I doubt that further examination of the small bowel by a barium meal would have led to the correct diagnosis. On these films there is excellent retrograde filling of the terminal ileum, and I should say again, even in retrospect, that the mucosa appears normal.

DR. SARRIS: Do you now believe that the serrations represent ulcerations?

DR. LINGLEY: They undoubtedly do.

DR. ALFRED KRANES: I should like to ask Dr. McKittrick why he considered this to be an early case of regional ileitis. What about the history of diarrhea five years previously? We know very little concerning the natural history of this disease.

DR. MCKITTRICK: I confess that I used the adjective "early" to signify not the duration of the disease but the degree to which the pathologic process had progressed. The disease may well have been present five years, but it had not yet appreciably narrowed the lumen of the bowel.

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The Journal does not hold itself responsible for statements made by any contributor.

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HALF A MILLION TYPEWRITERS

It is an interesting commentary on the magnitude of the enterprise in which we are currently engaged that the City of Magnificent Distances, wherein is lodged the very nerve center of our efforts, has issued an appeal for five hundred thousand used typewriters. It seems incredible that there should be so many key positions.

One of the inalienable rights of a democracy is that on going to war it should have two fronts —the aggressor nations, the professional fighters, avoid this until the last ditch, but we insist on having our real front and our paper front. The Battle of the Solomons has its quiet periods, but the Battle of the Bureaus never ceases.

There has been some sniping lately on the latter front, which seems to be one of bureaucracy versus the business of the Nation, — and that business at the moment is war and war production, — and a few of the absurdities of how a bureau does its work have been pointed out. The story has been told, for instance, of the "tired businessman," trying to consummate a contract with a departmental office in Washington, who was required to obtain fifty-one signatures for his papers. And a federal co-ordinator has been defined as one who brings organized chaos out of regimented confusion. Then, the *Reader's Digest* gives us the story of a subordinate in the War Department, enthusiastic and therefore probably young, who suggested the destruction of a large accumulation of tattered and obsolete records. The written proposal went up the line from one office to another until it, too, like a rolling snowball, had acquired a formidable bulk of its own. Approval after approval was attached to it until finally it reached the ultimate authority; permission was given to burn the papers — provided that copies were made of all those destroyed.

The *Journal of the American Medical Association* takes strong editorial notice in its November 7 issue of the report of Senator Pepper's Subcommittee on Manpower of the Senate Committee on Education and Labor. Apparently ignorant of the inventories of available medical personnel made by the American Medical Association in 1940 and by the Procurement and Assignment Service in 1941, the committee proposes the establishment of still another civilian authority to supervise and control the drafting and recruiting of physicians. So do republics stagger and fall under the burden of their own accumulated processes of government.

Typewriters, we know, are a necessary part of the equipment of our navy from dockyard to submarine; our military establishments need them from Ayer, Massachusetts, to Sydney, Australia; on our far-flung battle lines their keys, poked by the ponderous forefingers of countless staff sergeants, crackle above the staccato notes of the tommy guns; and that is where they should go. If they are wanted mainly in the Nation's capital,

however, and if, as has been suggested, the true purposes of democracy are being buried beneath a mass of protocols, then the need for half a million typewriters reveals, as Mr. Churchill would say, the very belly of the monster.

THE DOCTORS MAYO

A WIRY little man of English, Flemish and French Huguenot ancestry born in the neighborhood of Manchester, England, the son of a sea captain, having pursued a medical education in Manchester, Glasgow and London without staying long enough to get a diploma, decided at the age of twenty-five to try his fortunes in America. This was William Worrell Mayo. He was a pharmacist in Bellevue Hospital, New York, in 1845; he followed the westward trek to Buffalo, thence to Indiana where, in Lafayette, he opened a tailor shop, and then pursued medicine again and received a degree in 1850 from the Indiana Medical College at La Porte. "He was never satisfied with things as they were, but always wanted to go further," wrote his son later. Accordingly, with his Scottish-American wife, he went on to St. Louis, where he obtained a medical degree from the University of Missouri, and to St. Paul; he explored the new settlements in the Lake Superior district, was attracted by the fertile valley of the Minnesota River, became purser on a river steamboat and publisher of a newspaper, manufactured patent medicines, and settled for a time and began the practice of medicine in Le Sueur, where, on June 29, 1861, was born a son, christened William James. He failed to get a commission in the Civil War, but was in the thick of the defense of the frontier settlements in the Sioux uprising and was foremost in the care of the wounded. Finally, in 1864, attracted by the boom town of the new wheat country, he moved to Rochester, where, on July 19, 1865, a second son, Charles Horace, was born.

Dr. Mayo became the horse-and-buggy doctor of the district — active, enterprising and ambitious. He used a microscope, gathered a library, organized medical societies, went on study trips to New York and Philadelphia and returned to practice the new surgery. For the two sons, the life was that of country boys: school, chores, sport and, especially, helping their father with his work. "It never occurred to us that we could be anything but doctors." Will went to the newly founded medical school of the University of Michigan at Ann Arbor, where his career was not impressive. Six years later, in 1888, Charlie graduated from the Chicago Medical College (affiliated with Northwestern University), where he sat under Senn, Fenger, Andrews, Davis and Dudley — good teachers and, fortunately, converts to Listerism. Without the advantage of hospital internships, the boys went back to Rochester to help their father. To young Dr. Will is attributed the statement: "I expect to remain in Rochester and to become the greatest surgeon in the world."

The "old doctor," as he was then called, had become the most widely consulted surgeon of the region. He had operated on thirty-six ovarian cysts, with a mortality of 25 per cent. He had not adopted Listerism.

Young Dr. Will made trips to New York for postgraduate study, watched the work of Sands and Gerster, became convinced of the value of Listerism, and brought it back to Rochester. In 1883, a tornado swept the town, and the total lack of facilities for care of the wounded, who had to be placed in a dance hall, suggested to Mother Alfred of the Sisters of St. Francis the need of a hospital, which was duly built (it is said against the advice of Dr. Mayo). Thus was founded St. Mary's Hospital, with the "old doctor" as consultant and the sons in active charge.

It is impossible to trace adequately the growth of the Mayo enterprise. At first, the brothers assisted each other without specialization, but gradually Dr. Charlie took charge of diseases of the eye, ear, nose and throat, bones, joints, nervous system and thyroid gland, and Dr. Will covered the abdomen, pelvis and genitourinary system. Sister Joseph succeeded Mother Alfred and, besides having general charge, acted for years as

Dr. Will's first assistant at operations. Dr. Stinchfield, a local practitioner, was associated in the medical field, and later Dr. Christopher Graham. The sick and injured of a wide and increasingly populous countryside, having no nearer consultants than the Twin Cities, flocked to Rochester. Associates were added to the staff whose names are almost as familiar as their chiefs': Plummer, Judd, Wilson, MacCarty — to mention but a few of the older group. Addition after addition was made to St. Mary's, laboratories were established, hotels erected and used in part as hospitals, specialties inaugurated, and new office facilities and ambulatory clinics provided. In 1912, a system of fellowships was devised through which young graduates — on moderate stipends — could observe, learn and provide services. In 1915, a million and a half dollars was appropriated from surplus earnings to create the Mayo Foundation for Medical Education and Research, as a graduate department of the University of Minnesota, and four years later all the assets of the Mayo Clinic were conveyed to a trust to provide for the perpetuation of the clinic. The last great physical expansion was the completion of the new clinic building in 1938 at a cost of three million dollars — a skyscraper of fifteen stories surmounted by a bell tower with a carillon. In that year, Dr. Will ceased operating, and a year and a half later, a retinal hemorrhage wrote finis to Dr. Charlie's surgical work.

There is no mystery in the success of the Doctors Mayo. "Stress the unusual opportunity that existed in the time, the place, the general setup, not to be duplicated now," said Dr. Will, in authorizing the work. Health, ability, ambition, industry and fair dealing were basic elements. The peculiar traits and capacities of the brothers were complementary. From the first, they were systematic in visiting medical centers and bringing back whatever was worth while, and in supporting organized medicine and attending society meetings, presenting papers and participating in the discussions. They were frequent visitors to the clinics of McBurney, Bull, Abbe and Weir in New York; Price in Philadelphia; Fenger, Ochsner, Senn and Murphy in Chicago; Osler, Welch and Halsted in Baltimore; and Cheever, Warren, Cabot and Richardson in Boston. Constantly, they communicated to medical journals their experience, which was usually greater than that of others. They made full use of all ethically permissible methods of publicity, and were unfairly blamed accordingly. The financial return was large, but it is stated that 25 per cent of their patients paid nothing, 30 per cent paid the bare cost, and from 45 per cent came the professional fees, which in the end, in the form of endowments for research and education, were "turned back to the People from whom it came."

Miss Clapesattle, editor of the University of Minnesota Press, to whom the writing of the Mayo biographies* was entrusted, has produced a work — almost monumental in character — covering a far wider field than the biography of three physicians. Its pages represent prodigious bibliographic research, documented in a section at the end of the narrative text. Each phase of the career of the three doctors is pictured in a setting of the locale and contemporaneous events, affording a usually interesting and often very valuable historical background: the founding, in 1903, of the Society of Clinical Surgery — the model for all peripatetic clinical groups; the beginnings and course of specialization at the clinic, the additions to the staff, the growth of laboratory work, and the undesired publicity thrust on the brothers and the accusations of unethical conduct that beset them; and the part played by the clinic in World War I.

Among the million patients who passed through the Mayo Clinic, among the uncounted friends in and out of the profession, among students and historians of the medical scene, there will be thousands who will read every word of *The Doctors Mayo* with intense interest. For the average reader, both lay and medical, the book is too long, too detailed, too anecdotal, too full of trivialities. There are occasional lapses from the canons of good taste, occasional inaccuracies and interpre-

*Clapesattle, H. *The Doctors Mayo.* 822 pp. Minneapolis: University of Minnesota Press, 1941.

tations of dubious validity, and rare mistakes. But these criticisms are in themselves trivial, and one can only admire the work of Miss Clapesattle in her portrayal of these three beloved physicians.

MEDICAL EPONYM

Southey's Tubes

These tubes are described by Reginald Southey (1835–1899) in the report of a case, "Chronic Parenchymatous Nephritis of Right Kidney: Left kidney small and atrophied — old scrofulous pyelitis," which was read before the Clinical Society of London on April 27, 1877 and which appears in the *Transactions of the Clinical Society* (**10:** 152–157, 1877). A portion of the article follows:

> I determined to endeavour to relieve her dropsy by mechanical means, and to this end employed an apparatus which is, I believe, novel in England. I had a small trochar made, with tiny well-fitting canulas, but little larger than the ordinary subcutaneous injection needles; these canulas, instead of terminating with a protecting rim, end with a little bulbous extremity.
>
> They are inserted into the subcutaneous cellular tissue with great facility, and with no more pain than the ordinary needle-prick produces; the canula, inserted parallel to the surface, is left stuck in the skin; and a long, fine capillary indiarubber tubing is now drawn over the protruding bulb and tied *in situ*. This tying in of the canula is not essential or even often necessary.
>
> The long ends of the capillary tubes are now carried outside the bed and into a pan beneath it, into which the serous dropsical fluid drips or drains away.
>
> One drainage canula was inserted into each leg, and through the two tubes about 2½ pints, or, in fact, 71 ounces, of dropsical effusion drained away each 24 hours, with considerable relief, of course, to the tension.

R. W. B.

MASSACHUSETTS MEDICAL SOCIETY

COMMITTEE ON ARRANGEMENTS

Owing to the restrictions on gasoline and train travel and to the scarcity of hotel accommodations in Springfield, the Committee on Arrangements will recommend that the Council rescind its vote of May 25, 1942, whereby Springfield was designated as the place of the annual meeting in 1943. This committee will further recommend that the annual meeting in 1943 be held in Boston on May 25 and 26. Both recommendations have been endorsed by the Executive Committee.

Gordon M. Morrison, *Chairman*

STATED MEETING OF THE COUNCIL

A stated meeting of the Council will be held in John Ware Hall, Boston Medical Library, 8 Fenway, on Wednesday, February 3, 1943, at 10:30 a.m.

Business:

1. Call to order at 10:30 a.m.
2. Presentation of record of meeting held October 7, 1942, as published in the *New England Journal of Medicine*, issue of November 12, 1942.
3. Report of Auditing Committee and of Treasurer.
4. Reports of standing and special committees.
5. Appointment of Delegates.
   (*a*) To the House of Delegates, American Medical Association, for two years from June 1, 1943.
   (*b*) To the annual meetings of the five New England state medical societies in 1943.
   (*c*) To the Annual Congress of the American Medical Association on Medical Education and Licensure at the Palmer House, Chicago, February 15 and 16, 1943.
6. Such other business as may lawfully come before the meeting.

Michael A. Tighe, M.D., *Secretary*

The two following reports are submitted for the advance information of members of the Council.

Report of the Committee on Finance

The Committee on Finance, after some preliminary correspondence, met on December 10, on which date the various committees are obliged by the by-laws to have turned in their estimates for the coming year. There were present Drs. Charles F. Wilinsky, Peer P. Johnson, Ernest L. Hunt, Edward J. O'Brien and John Homans. The Treasurer, Dr. Butler, was prevented by illness from attending. His absence made much of our information concerning the expenditures for the past year uncertain.

The committee had been informed, however, by Dr. Butler that the income and expenses of the Society for the year 1942 were likely to balance fairly closely. In other words, there was little likelihood of a favorable surplus such as had been secured in previous years. In 1942, the loss in dues, owing to the entrance of members into the military services, was beginning to be felt. But the Society should still have enjoyed an income from dues of something like $55,000. To this about $3000 income from invested funds should be added, making roughly $58,000 in all. Much of this is guesswork, since the Treasurer's books are not made up until the first of the new year. Very likely, if the income and outgo nearly balanced, the income was considerably less, since the budget of $50,800 could hardly have been overspent by any considerable amount. Owing to the establishment of the Blue Shield, the Committee on Public Relations exceeded its budget by about $1000; and the Secretary was obliged to exceed his budget by over $1300 on account of the new by-laws and other extras. However, the Committee on Arrangements made $3000, which more than balances these sums; the Committee on Publications,

through the *Journal*, will probably have saved several thousand dollars; and, in general, there was about the usual small saving within the estimates.

The budget for the coming year is made up on the basis that the Society should receive from dues only about $44,000. This takes into account a loss of $13,000 from the $57,000 that might have been received had the full membership paid its $10 dues. Probably this estimate of $44,000 is an optimistic one, for now that the district treasurers are no longer collecting the dues, difficulty in collection may well be encountered. However, to the $44,000 should be added about $3000 of income from investments, making perhaps $47,000 in all.

The budget is appended. It has been impossible to secure itemized accounts of last year's expenses. Even the gross sums expended are uncertain. However, whenever these sums are available, they are included. The items for the expenses of the Society's officers are recorded, as well as those of the committees that expend such sums as require itemization, according to the new by-laws. The budget of the *Journal*, as submitted by the Committee on Publications, is separately given.

There are some changes as compared with the budgets of previous years; furthermore, there are several changes as compared with the report offered to the Executive Committee on December 30. In the original report a sum of $3500 was allotted to the salaries of the treasurer and assistant treasurer. Dr. Butler, as many of you have heard, has asked for an indefinite leave of absence. Therefore the salary of the assistant treasurer is placed at $2000. At the same time, the more elaborate bookkeeping required by the by-laws and the expense of collecting the dues has called for an increase in the budget of the treasurer's office from $400 to $1750, the latter being $800 greater than the sum originally suggested to the executive committee. The sum of $900 was found to be required for the expenses of the delegates to the House of Delegates of the American Medical Association. And, finally, the amount requested by the Committee on Arrangements has been raised from $100 to $500, owing to the decision to shift the place of the annual meeting from Springfield to Boston and the resulting increase in expenses. This committee has a separate budget, the details of which are not included.

The expenses of the Secretary's office have gone up from $1800 to $2500. This increase is due to the increased activities of various large committees. There is a question whether some of the these committees should not assume part of this expense, but this seemed to the Committee on Finance to be merely a question of bookkeeping.

The district treasurers no longer get their honorarium of $2700.

The supervising censors may require $100 for holding two meetings. Fifty dollars for each may represent their expense of attendance.

The *Journal* is slowly becoming less of a financial burden to the Society. Under Dr. Nye's guidance, its subscription list has steadily increased. Each year it has turned back several thousand dollars out of its budget of about $20,000. Even with the war changes, the Committee on Publications expects it to cost less than $15,000 and has asked for a budget of that amount.

The Committee on State and National Legislation, which, in 1941 (the last year the Great and General Court met in Massachusetts), spent over $3500, is asking for $1800. This is itemized fairly completely, except for the fees of legal counsel; yet it seemed to the Finance Committee that this was a reasonable sum.

Putting this all together, the Society ought to squeak through this coming year. It may well have to spend some of its principal. However, there does not seem to be any objection, at times like these, to doing so. The uncertainty concerning the future of invested funds should influence the Society to spend its income rather than pile up principal. To be sure, if the Treasurer had not saved more than $25,000 in the last five years, it might have been less ready to turn over this sum as a backlog for the Blue Shield. But barring such uses as this, there seems nothing at the moment for which the Society should lay up its principal. In this connection, it may be well to consider the $60,000 or so that is set aside at compound interest for the "permanent home." Is this being used to the best advantage?

JOHN HOMANS, *Chairman*
ERNEST L. HUNT
PEER P. JOHNSON
EDWARD J. O'BRIEN
CHARLES F. WILINSKY

* * *

BUDGET FOR 1943

The following appropriations are recommended:

BUDGET 1942		BUDGET 1943
	SALARIES	
$3000	Secretary	$3000
3000	Executive Secretary	3000
2000	Treasurer and Assistant Treasurer	2000
	EXPENSES OF OFFICERS AND DELEGATES	
500	President and Vice-President	500
1800	Secretary	2500*
400	Treasurer	1750
2700	District treasurers	0
750	Censors (supervising)	100
400	Delegates to House of Delegates, A. M. A.	900
4500	Society Headquarters (general expenses)	4500*
200	Shattuck Lecture	200
450	Cotting Luncheons	450
125	Executive Committee	500*
	STANDING COMMITTEES	
100	Arrangements	500
60	Ethics and Discipline	60
25	Finance	25
2000	Medical Defense	1500*
0	Medical Education	0
10	Membership	100
0	Society Headquarters	0
	Publications:	
20000	*New England Journal of Medicine*	15000*
2100	Directory	0
25	Public Health	25
50	Industrial Health	50
	SPECIAL COMMITTEES	
100	Legislation	1800*
5	Committee to Examine W. P. A. Records	5
150	Maternal Welfare	150
1000	Public Relations	600*
1000	Postgraduate Instruction	200
0	Military Postgraduate Instruction	350*
300	To Revise By-Laws	0

50	Tax-Supported Medical Care	0
0	Cancer Clinics	0
0	Postpayment Medical Care	0
	Ways and Means to Conserve Doctors' Energies during War	0
4000	Returns to District Societies	4000
$50800		$43765

*Itemized below.

Detailed Expense Accounts

Exp. 1942		Est. 1943
	Secretary	
$993	Clerical	$1000
369	Postage and mailing	370
1337	Printing	600
306	Stenographic reports of council meetings	200
	Telephone	75
	Miscellaneous	50
	Treasurer	
	Clerical	1000
	Postage	200
	Stationery	50
	Clerical in connection with dues	500
	Society Headquarters (principally rent to Boston Medical Library and many complicated relations with *Journal* for various services)	
	Executive Committee	
	Clerical	200
	Expense of attending meetings	300
	Committee on Medical Defense	
572	Legal fees (not split up)	1500
197		
625		
	Committee on Legislation	
	Legal counsel	750
	Legislative reporting service	300
	Expense of attending meetings	350
	Copies, *Who's Who in Legislature*	50
	Clerical (headquarters)	100
	Telephone and telegraph	100
	Stationery, postage and incidentals	150
	Committee on Public Relations	
	Clerical	300
	Expense of attending meetings	300
	Committee on Military Postgraduate Instruction	
	Travel expenses (speakers)	200
	Telephone and telegraph, correspondence	75
	Expense of attending meetings	50

New England Journal of Medicine

Actual and Estimated Figures on Operation

	Actual 1941	Estimated 1942	Actual 1942*	Estimated 1943
Revenue				
Advertising	$26,400	$27,000	$27,600	$28,000
Engraving	1,400	1,500	1,700	1,500
Reprints	7,500	7,300	7,300	6,500
Subscriptions	20,400	21,000	23,700	24,500
Miscellaneous	800	800	900	800
	$56,500	$57,600	$61,200	$61,300
Expense				
Publication of *Journal*	$39,600	$43,000	$43,400	$42,000
Publication of reprints	5,200	5,000	5,700	5,000
Office and other salaries	21,400	22,500	21,500	22,000
Commissions, fees and so forth	3,300	3,300	3,700	3,600
Office and sundry expenses	3,500	3,500	3,500	3,500
	$73,000	$77,300	$77,800	$76,100
	56,500	57,600	61,200	61,300
Loss	$16,500	$19,700	$16,600	$14,800
Appropriation	$20,500		$20,000	$15,000

*Based on ten months' operation.

Report of the Committee on Education

As a result of a suggestion from the Executive Committee on June 24, 1942, we undertook an investigation of the nursing situation that has been created by the war. The subject proved to be so complicated that we made only a preliminary report to the Council in October (*New Eng. J. Med.* **227**:753, 1942). We have held five formal committee meetings, at one of which Miss Goostray, of the Children's Hospital, Boston, president of the National League of Nursing Education, was present, and at another Dr. Faxon, of the Massachusetts General Hospital. Dr. A. William Reggio and Dr. Charles G. Mixter gave a great deal of time to us and were present at one meeting. Dr. Mixter also sponsored a dinner discussion, which was attended by sixteen heads of hospital services in and around Boston. We have had many consultations with Miss Carrie Hall, Miss Katherine Shepard, Dr. N. A. Wilhelm, Dr. Dwight Siscoe, Dr. Charles Lawrence, Mr. Frederick Ayer, Mr. R. M. Bradley and many teachers and practitioners of medicine. We have had fruitful correspondence with various superintendents of nursing schools and hospitals, the Army Nurse Corps and the British Information Service; and we have studied material that has been published in the *American Journal of Nursing* and in the *Nursing Information Service*. We now present the following data and discussion for the information of the members of the Massachusetts Medical Society as a basis for current and future action.

The need of our armed forces for an estimated 60,000 graduate nurses has caused a great drain on hospitals and the civilian agencies. Army authorities have expressed concern over the possibility of failure to meet their needs on time. Civil officials have likewise become aroused over the dangers to the home population by the removal of so many skilled workers particularly in the event of an epidemic or widespread disaster. The medical profession should be acquainted with the facts that are available so that it may take the lead in whatever adjustments are deemed necessary, since physicians direct the nursing care of their patients and know best which changes are safe and which are not.

Nursing service is rendered by five categories of individuals. The first four are registered nurses, licensed attendants (practical nurses), Red Cross volunteer aides and ward helpers. The fifth group consists of those relatives and friends of patients who help out as a matter of course; since they are unorganized, untrained and unpaid, and work in specific situations as the needs arise, their value cannot be weighed in a study of national and community problems and they will not be mentioned hereafter. The first category is most important because only registered nurses are acceptable for service in our armed forces and in large hospitals and public-health and community-health agencies. Their large diversion to the war effort, however, has given more importance to the licensed attendant and to other auxiliaries, both paid and volunteer.

The following notes describe briefly the duties and the present situation of each group rendering nursing service.

Registered nurses. A nurse is defined (House Bill 858 [Mass.], January, 1939) as follows:

> A nurse performs any professional service requiring the application of principles of nursing based on biological, physical and social sciences, the responsible supervision of a patient requiring skill in observation and interpretation of symptoms and reactions and the accurate recording of facts, the carrying out of treat-

> ments and medications as prescribed and directed by a person licensed to practice medicine, and the application of such nursing practices and procedures as involve an understanding of cause and effect in order to safeguard the life and health of a patient and others.

In other words, she is a woman (or man) of good education who has been given three years of intensive training in the basic medical sciences and in the care of patients under the constant supervision of nurse educators, medical educators and interns. She is a woman of a certain maturity, responsibility and independence. These qualities make her desirable for Army service, where situations may arise that call for rigid discipline as well as judgment and initiative. She works best on acutely ill patients in hospitals and homes, and in executive and administrative posts in hospitals and public-health agencies, and as a staff nurse. Her shortcomings are those that might be anticipated because her experience is limited to work in large hospitals filled with surgical and critically ill medical cases; she is often unwilling or unable to do cooking and housekeeping (this fault is not confined to this class of nurse); she is unhappy in caring for patients with chronic disease and for well babies; and she shows signs of being a specialist.

Several estimates of the number of registered nurses in this country have been recently made. They vary considerably. No conclusion can be reached by adding up the number of graduates of nursing schools in the last twenty or thirty years for several reasons: some graduates (7 per cent or more) do not take or pass state registration examinations or National Red Cross standards; many get married (the marriage rate for all nurses under forty is 48.4 per cent); and a few abandon their careers for other types of work, although some return as their circumstances change or the demands for service increase. The most authoritative recent survey is the National Inventory of Registered Nurses in 1941, which was summarized in the *American Journal of Nursing* (42:769–773, 1942) by Pearl McIver. A questionnaire was sent to the 369,287 nurses listed in the 1940 census. Answers were received from 289,286, of whom 173,055 (60 per cent) were engaged in practice. If those who did not reply are rated as inactive, then only 45 per cent of the total number were active. However, of the 116,231 inactive nurses who returned their questionnaires, 25,252 (22 per cent) stated that they were available for duty in case of need. In other words, in January, 1941, there were 198,307 registered nurses active or available in the United States. Approximately 50,000 nurses have been graduated in the subsequent two years. A second inventory has just been authorized to bring the statistics up to date.

Of the employed nurses in the 1941 inventory, 81,708 (47 per cent) worked in institutions, 46,793 (27 per cent) were on private duty, 17,766 (10 per cent) were in public-health positions, 5512 (3 per cent) were in industrial plants, and the other 13 per cent held miscellaneous or undescribed jobs. Nurses who were unmarried and under forty years of age numbered 98,693. Estimating physical disabilities at 20 per cent, it was probable that at that time (January, 1941) there were 75,000 to 80,000 nurses available and acceptable for war duty. This number has been increased by the graduation of several classes since, and by the recent Army rulings that married nurses are acceptable if they are not with their husbands and if they are willing to go anywhere and that women up to forty-five years of age may be acceptable.

These statistics clearly show that there are enough registered nurses to meet the demands of our armed forces. But they are not being met. Figures given out by Miss Marian G. Randall, chairman of the Inventory Committee of the governmental Subcommittee on Nursing, showed 30,000 nurses in the Red Cross First Reserve in April, 1942. The monthly quota of 3000 since that time has not been reached. How serious the deficit is cannot be estimated, for exact figures are withheld on grounds of military expediency. The various states, in April, 1942, had contributed from 13 to 60 per cent of their quotas; Massachusetts was credited with 1206, or 20.5 per cent of its quota.

The military authorities are disturbed by this inadequate response. The American Nurses' Association, in co-operation with the League of Nursing Education and the Red Cross Nursing Service, early last year set up a committee, known as the Nursing Council on Defense, in each state. Since Pearl Harbor, the title has been changed to Nursing Council for War Service. These committees have been very active in securing nurses for the Army and Navy and in aiding in the major readjustments that have been forced on civilian hospitals, industrial plants and public-health and civilian-defense agencies. However, they do not have enough power to be effective. A serious shortage of nurses is reported from various parts of the country. The average hospital has lost only three or four nurses; but many state and mental hospitals and some metropolitan hospitals have suffered severely. Moreover, population shifts resulting from the establishment of war-industry plants have not been met by changes in nursing ratios.

The problem has many sides and is being met by a number of solutions. An obvious first step is now under consideration — that of fashioning an agency with power to induce nurses who should join the armed forces to do so, and with power to allocate important nursing teachers, supervisors and administrators to their jobs so that essential teaching and hospital services will not be stripped. Another step that provides quick results is the recall of inactive nurses. As noted above, more than 25,000 trained women indicated last year their willingness to return to duty should the need arise, and they are doing so. More than 700 have come back in Massachusetts, and the Committee on Public Safety, in co-operation with nurses' organizations, is striving to get others. It is obvious that service means dislocation of family life and jobs to many of them. Some are serving at considerable personal sacrifice; others can give only part of their time. The same is true for those who are handicapped by physical or age infirmities. Hospitals gladly make allowances for such factors. For those who need to brush up on recent nursing procedures, refresher courses have been given with federal grants-in-aid. More than 500 have attended courses in this state in the past year. However these reactivated nurses can take care of only a small fraction of the present deficit. It is clear that more nurses must be trained, as many and as soon as possible.

There has been a marked increase in the number of pupil nurses in accredited nursing schools in the United States in the last few years. There were about 79,000 of them in 1929, an average of 70,000 yearly in the next decade, and then a rise to 82,000 in 1939, 85,000 in 1940, 87,588 in 1941, and 91,457 in January, 1942. Thus there has been an increase of 11 per cent since 1939. Admissions in 1942 have been approximately 49,000, or 18 per cent more than in 1941. But authorities in Washington had set 55,000 admissions as the goal for this year. It was not reached in spite of an intensive campaign of adver-

tising and interviews in schools and colleges. Does this mean that only 50,000 young American women can be yearly induced to take up nursing? Some nurse educators are inclined to believe that this is a saturation point for the profession. Or does it mean that many who might enroll do not yet realize the need for nurses? Or that they are more attracted to the WAACs and the WAVES and defense industries, which have more to offer financially and patriotically in immediately useful war work?

Answers to these questions will influence greatly the educational plans now under advisement. Schools of nursing have been criticized for rejecting applicants on the ground that unduly rigid entrance standards are responsible for the shortage of pupils. That this is not so is shown by the fact that about one third of the women who enter nursing schools leave before their three years are up, according to figures published in the pamphlet "Facts about Nursing," issued by the Nursing Information Bureau in 1941. It appears that the greater part of this considerable wastage represents changes in career (marriage, industry). Scholastic failures are relatively few. More lenient admission policies would undoubtedly only increase the wastage. With the continuance of this loss, it is estimated that 26,000 to 28,000 nurses will be graduated in each of the years 1942 through 1944. Surely the totals are not large enough to warrant optimism concerning their adequacy in meeting the Nation's needs for war and for the care of the civilian population.

A few remarks on nursing schools may be pertinent at this point. There are 1300 accredited nursing schools in the United States. They are run by educators of ability, and they have drawn freely from the pedagogical wisdom of schools and colleges. Their standards are subjected to frequent review by the National League of Nursing Education and the state boards of nurse registration. Legal requirements for registration of graduates are quite uniform. Good moral character is universally demanded. Four years of high school as preliminary educational background are required by forty-four states. Training must be of three years' duration in forty-three states, but fourteen (including Massachusetts) allow six to twelve months' credit for college work. Age at registration must be at least twenty-one in forty-three states. The structure of the courses and the requirements for practice are the outgrowth of many years of experience on the part of those who have worked constantly with nurses. Therefore any suggestions concerning their alteration because of the war emergency should get the consent and co-operation of informed sources before they are put into effect.

An increase in the number of training schools waits on proof that existing schools cannot take care of the applicants for admission and on proof that the proposed new schools can provide facilities for turning out graduates acceptable to the boards of registration. The trend of the past decade has been toward fewer and better schools, similar to the trend in medical schools a generation ago. Schools have been asked to admit three classes annually as another way of accelerating production. Naturally the decision to do so must rest with the individual school according to the best method it finds of handling its teaching, housing its students and caring for its hospital patients.

We have listened to much criticism of the registered nurse and her school. We are told that she knows both too much and too little, that she wants to be a specialist, that she dislikes work outside hospitals, that she is unwilling to do housework and cooking and so forth. All of us have had disagreeable experiences with this sort of nurse. Nurse educators freely admit her existence. We have also heard it asserted that schools teach much that is unnecessary, beyond the pupil's grasp, and in a too rigid and complex fashion. Again, responsible nurse educators agree in part, and point to their frequent consultation with pedagogical experts and their constant revision of curriculums. Recently in this state, a review of the contents of the various courses was begun at the direction of the State Board of Nurse Registration and the Nurses' Association and with the advice of physicians in the several specialties. But does it follow that better nurses can be produced if they are not taught so much and in a shorter time?

It does not seem wise to lower the entrance requirements for pupil nurses, for a high-school background is essential, and a college course desirable, if they are to absorb the training that they are offered. Furthermore, the quality of a product depends not only on the quality of the material that is put into it but also on the time that is allowed for its growth. Judgment, medical insight and discipline take time to ripen. More can be expected of a nurse trained for three years than of one trained for one year. Nurses are what they have become today not because they have banded together in an exclusive guild that relegates the interests of patients and physician to a position below their own. They are what their employees, the physicians, have helped them to be. The medical profession has fostered their development as anesthetists, operating-room assistants, administrators and research aides; every year it adds to their tasks more tests and treatments that doctors only were accustomed to perform. This tendency has increased as the shortage of physicians has grown, and nursing schools must continue to supply the demand. Military authorities show their approval by accepting only the three-year-trained nurse. Nurse educators resist the demand for thoughtless mass production, pointing to the unfortunate situation that followed World War I when many hastily trained nurses were thrown on the market who, unable to meet the requirements of boards of registration, practiced an inferior brand of nursing that reflected on the profession and themselves. English representatives, who have seen their country struggle with a mass of volunteer and partially trained workers in the last three years, have urged us not to lower our standards for those who must supervise auxiliaries.

It comes down to this — one type of nursing school cannot produce all types of nurses. Nurses for general and home duty can be trained in a year or so by schools for licensed attendants as discussed in the next section. Nurses for special hospital and war service must continue to be trained by the schools of nursing. No shortening of the duration of their course should be recommended, since this would interfere seriously with the quality of the graduates. The three-year course cannot be condensed by the elimination of vacations, as the medical-school course has been, for nurse pupils get only three weeks' vacation each year. We do not feel competent to pass judgment on the possible elimination of subjects or of hospital affiliations for the same purpose, but we can see disastrous effects on hospitals that have come to rely on the services of pupil nurses in the care of their patients if those services are taken away from them. The League of Nursing Education, aware of the critical shortage of nurses and the factors discussed above, has made certain suggestions in co-operation with the Office of Civilian Defense and

the Sub-Committee on Nursing in Washington. The following is quoted from the *American Journal of Nursing* (**42**:1182, 1942):

> While emphasizing the importance of maintaining adequate preparation, the Board [of Directors] recognizes that civilian hospitals are becoming more and more dependent on student nurses to care for their patients and to be ready for civilian emergencies. In view of this situation, therefore, the Board recommends:
>
> 1. That schools offering the three-year curriculum plan to complete within thirty months all organized instruction and clinical experience in at least the four major services, medicine, surgery, obstetrics and pediatrics, leaving six months free for supervised practice wherever needed in the hospital. This arrangement would also make it possible, should a plan be worked out in co-operation with Army and Navy hospitals, for students who choose to go into military service, to have such an affiliation during this six months; or later if the need becomes more acute, students might be released to enter military service at the end of 30 months.
> 2. That, where state laws permit, an accelerated program be planned for students admitted with two to four years of approved college preparation which would make it possible for such students to graduate at the end of 24 to 28 months. The length of time should be determined on the basis of the previous educational preparation of the student and her level of achievement in the school.
> 3. That schools of nursing critically examine their curricula and eliminate duplication in instruction and non-essential activities, giving emphasis to those elements in the curriculum that are most vital in terms of present and probable future needs.
> 4. That every effort be made to extend the use of auxiliary personnel in so far as this can be done with safety to the patient.
> 5. That in view of the greatly enlarged numbers of student nurses and auxiliary personnel in hospitals, definite measures be taken to retain and stabilize teaching and supervisory staffs to provide for the adequate preparation of students and the proper supervision of auxiliary workers.

A few final comments on the efficient use of the present store of nurses remain. Private-duty nurses must be prepared to render any service necessary in homes. "Luxury nursing" is out for the duration of the war. Patients must accept the decision of the hospital administrator and the clinical staff whether they need special nurses, and for how long, regardless of their ability to pay. The sharing of a special nurse by several patients has been tried and the experiment has failed, owing to personal difficulties. Hospital authorities have been asked to "alter their personal policies in ways which will encourage graduate nurses to remain in institutional service." This is a cautious expression of the fact that hospitals must pay their nurses enough to meet the competition of industrial nursing and non-nursing war work. Furthermore, the Congress of the United States appropriated $1,800,000 in 1941 and $3,500,000 for 1942 and 1943 for nursing education, these funds to be used to assist nursing schools to expand their teaching facilities and as scholarships for young women needing financial aid in undertaking a professional course.

Licensed attendants. A licensed attendant is defined in the law (Chapter 620) enacted in Massachusetts in January, 1942, as one whose purpose is "to care primarily for convalescent or chronically ill patients or those suffering from minor ailments, in hospital or home, under the supervision and direction of qualified physicians" and "to assist registered nurses in the care of acutely ill patients in hospital or home, under the supervision and direction of qualified physicians." This law attempts to regularize a miscellaneous group of nurse workers for the protection of the public. Some are graduate nurses who did not take or failed to pass registration examinations; others are graduates of unrecognized schools of nursing or graduates of good schools of practical or household nursing, or women self-taught or sketchily trained in nursing homes. All of them could be licensed to practice if they passed the state examination for licensed attendants by August, 1942; since that time, they must show that they have been graduated from attendant nurse schools approved by the state nursing authority. Since registration is so recent a development, there are no reliable figures concerning the number of these nurses in the United States that can be used as an estimate of the aid which they can give in the present emergency.

The foregoing definition shows that the licensed attendant is designed to supplement the services of the registered nurse and to render those that the registered nurse does not. She must know how to cook and how to manage a household; she must have the humility to be content with caring for patients with minor illnesses and for well babies; and she must have the patience and persistence to serve chronically ill or elderly patients for months or years. To fulfill these duties, she does not need to have as much preliminary education or as much training in school and hospital as the registered nurse. While her weekly wages are less than those of the three-year nurse, her annual income is often as great or greater. Practicing physicians know her value; in fact, they really prefer her services when they have problems such as those listed above. Leaders of the nursing profession also recognize her worth and have sought for many years to establish her on the sound educational and legal basis that has now been effected.

Reasons for the tardy recognition and utilization of the attendant nurse are many. An irritating but minor one is her competition with the private-duty nurse. It would seem that physicians could lessen this by a wise choice of the type of nurse they need for any particular case, and that nurses could do their part in fostering co-operation by granting the licensed attendant some degree of participation in the American Nurses' Association. Such a step would go far in promoting mutual understanding and respect and make less likely the development of a rival organization with contests concerning fields of interest. Large metropolitan hospitals have long refused to employ attendant nurses because they are not trained adequately to serve seriously ill patients and because pupil nurses can render all necessary services to the rest. Now, however, hospitals are so short of staff nurses that they have begun to use attendants on certain wards and in certain situations, and on the whole, the experiment seems to be working well. Emergency medical units and the hotel hospitals now organized by the Office of Civilian Defense include licensed attendants. Veterans' Administration hospitals should find many places for them. Public-health nurses are finding them useful in extending their services. It is likely that military authorities will be forced to call on them for work in their hospitals for wounded soldiers and sailors to relieve corps men. So it is obvious that a broad career is opening up for the licensed attendant.

Nevertheless, her chief usefulness, and her chief interest to us at this time, is in civilian community service, for in case of disaster or epidemic, the bulk of the medical work will be done in homes.

There are now in Massachusetts eight schools for attendant nurses — Beverly Hospital, Harley Hospital, Household Nursing Association, Holden District Hospital, North Adams Hospital, Tewksbury State Hospital, Waltham Training School, and Robert Breck Brigham Hospital. There are three types of setup for such schools. One is quartered in a chronic hospital (such as Tewksbury), with a practice house on the grounds for training in home cooking and management. Another is centered on the public-school system (as in the Rochester, New York, experiment). The third, which appears best, is that of the Household Nursing Association, which gives two months of preliminary training in its central group of buildings, affiliates with a number of small neighboring hospitals for twelve months of ward work, and then supervises work in actual homes for six months. The Massachusetts Approving Authority demands a minimum of twelve months' training. All these establishments are relatively inexpensive and should be multiplied throughout the State.

Long before Pearl Harbor, the far-sighted management of the Household Nursing Association made efforts to increase their enrollment. Their capacity with seven classes a year was 168, and their average pupil census was 125. They found that they could double this number without extending the hospital affiliations. The hospitals were so eager to secure the services of the pupils that they offered to pay the $60 tuition for all applicants who could not afford it. Yet their enrollment did not increase; in fact, there were, at the end of November, 1942, only 5 applicants for the December class, which normally numbers 18. They redoubled their efforts, with the aid of the Committee on Public Safety, and by advertisements and articles in newspapers, the radio and schools, with scanty results. As an example, one newspaper story netted several hundred replies, out of which came forty interviews and finally two unattractive applicants. Commissioner Downey informs us that efforts were made, a year ago, to enlist attendant-nurse pupils by talks by teachers and personnel advisers in various high schools throughout the State, but that the experiment was such a failure that it has not been continued. The Waltham Training School may be forced to close for lack of pupils, and the other schools are similarly affected. What are the reasons for this general lack of interest on the part of young (and middle-aged) women in attendant nursing? Are they not sensitive to calls for patriotic and community service? The most likely answer is that they can get better pay and more attractive work and hours in stores and manufacturing plants, which are calling even more loudly for them.

Certain lay leaders have proposed that, in view of the country's urgent need for nurses, we should concentrate on the development of the licensed attendant in all hospitals qualified to teach. They assert that these women can give satisfactory service and that hospital, nursing and military authorities should be forced to conform before it is too late. The proposals have been approved by some physicians and are the reason for this general report. The Committee on Medical Education finds them unsound on several counts. The most insurmountable obstacle right now is the failure, after considerable effort, to fill already established attendant-nurse schools, as noted above. Perhaps this could be done by some form of the draft, to which women are not as yet subject. But we doubt the workability of any scheme that would force people to perform tasks in which they are not interested. It might be that a section of the WAACs and the WAVES could be allocated for nurse training and duty in specific situations; it would be hard to apply them to civilian use. It is stated that more candidates could be obtained if they had the opportunity to train in large metropolitan hospitals. Attendant-nurse educators do not believe this. Furthermore, the quality of service that can be rendered by an attendant nurse is adequate only for chronic cases, the elderly, the well babies and children, and for simple household situations. We know that active-minded, eager women can be taught in a very short time to give excellent auxiliary aid and even to perform difficult nursing, medical and laboratory procedures. Such teaching requires a great deal of individual effort and supervision. The average pupil and the average class in any program of mass production respond to a much lesser degree; hence the necessity for the three-year program for turning out workers who can serve in acute medical and surgical cases and in military situations. Attendant-nurse and registered-nurse educators and hospital executives all agree that to use attendant nurses for cases beyond their ability is a sure way to invite disaster. Finally the establishment of two types of nursing schools in one institution is hazardous. The content and scope of the courses are necessarily different, so is the type of work on patients; and all this would lead inevitably to social and professional jealousies and friction, no matter how good the behavior of all, and impose a heavy additional burden of teaching and supervision on staffs that are straining every nerve to turn out the essential graduate nurse.

Red Cross volunteer aides. In 1941 the American Red Cross and the Office of Civilian Defense arranged a program for the training of volunteer nurses' aides. As it now stands, it gives women who are American citizens of good character and between the ages of eighteen and fifty, who have had a high-school education and who are physically fit and able to stand hard work, one hundred hours of training. Half this time is spent in classrooms, and half in hospitals under the supervision of nurses. After completing the course, the aides buy their uniforms and promise to serve a minimum of one hundred and fifty hours each year for the duration. Hours are quite elastic and not necessarily in one continuous stretch. In time of crisis, it is understood that the service may be longer and may be called for at distant points. It is women such as these (140,000 of them) that helped England immeasurably in these last three years. It was hoped that 100,000 of them might be trained in this country by the end of 1942. Actually this goal has by no means been reached (about 4000 exist in Massachusetts). Yet the results have been extremely gratifying from many points of view. About five hundred training chapters are functioning throughout the country; seventy-one hospitals are now teaching or available for teaching in Massachusetts. These volunteers are coming largely from an older group of women. They are wives and sisters of men in service; some are doctors' wives, schoolteachers and business women. They take their work seriously; glamour girls do not last. They have won the respect and admiration of nurses. Hospitals are eager to get them. They have done much for patients. They have become interpreters of medical, hospital and nursing needs to the community. They will be a real source of help in case of disaster or

difficulties arising from the loss of trained nurses to the armed forces. They are to be complimented and encouraged in every way.

Ward helpers. Ward helpers act as ward maids and run errands for patients and nurses. As the shortage of nurses has developed, they have been given minor duties in the care of patients. Essentially their jobs are similar to those of the Red Cross volunteer aides. They are more reliable for routine daily service because they are paid. It is foreseen that situations might arise calling for regular work on the part of the volunteers that they could not afford to give without recompense, since to do so would mean the loss of jobs or the disruption of family responsibilities. Therefore it is agreed that the volunteers may, in such circumstances, be paid, suffering thereby the loss of their uniforms and their amateur standing. Ward helpers usually are trained in the hospitals where they work. They can also be obtained from the Household Nursing Association, where they are given a one-month preparation course.

Ward helpers obviously are valuable to institutions but do not meet other community needs. To supplement the services of nurses and attendants in homes it is proposed that women able and willing to do household tasks freely or for hire, sign up with some central office, such as a nursing registry or a public-health agency. The proposal is certainly worth attention, although it is hard to guess what the response would be.

ROBERT T. MONROE, *Chairman*

COMMITTEE ON MATERNAL WELFARE

ANALYSIS OF CAUSES OF MATERNAL DEATH IN MASSACHUSETTS DURING 1941

ECTOPIC PREGNANCY

As has been customary in previous analyses, all cases of ectopic pregnancy are grouped under this specific heading, although in one sense they are surgical complications. There were 6 maternal deaths due to ectopic pregnancy during 1941, twice as many as occurred in 1940. One autopsy was performed.

The first case was that of a thirty-six-year-old primipara who began to stain when about two months pregnant and continued to do so for one month. She had had attacks of knifelike pain in the lower abdomen for the two weeks prior to hospital entry, and vaginal examination on admission showed that definite placental tissue was extruding from the os. A moderate amount of this tissue was obtained by curettage, and a firm mass was found in the anterior cul-de-sac, for which nothing was done. The following day the patient went into shock, and at laparotomy, the abdomen was full of blood, the bleeding arising from what was apparently a ruptured left tubal pregnancy. There was a hematosalpinx on the right. Bilateral salpingectomy was performed. Peritonitis developed and death resulted. Autopsy showed extensive hemorrhagic peritonitis. The ruptured tube did not reveal gross or microscopic evidence of ectopic pregnancy. This case was an unfortunate one. Intrauterine and extrauterine pregnancy existing at the same time are not uncommon; neither is it uncommon to have a ruptured tube due to ectopic pregnancy reported negative by the pathologist. Had this patient been operated on the day of the curettage, before rupture of the tube had taken place, in all probability the fatality would have been averted.

The second patient was a forty-three-year-old woman whose history is most inadequate so that her parity is in doubt. She was seen first when in a state of collapse and shock from abdominal hemorrhage; she was taken to the hospital by ambulance and died a few minutes after entry. The diagnosis of ectopic pregnancy with massive abdominal hemorrhage is probably the correct one; however, the medical examiner, who is said to perform no autopsies himself, refused autopsy in spite of the requests for one by the patient's physician and by the superintendent of the hospital where she died. One of the striking deficiencies of medicine in Massachusetts that has been brought out by the maternal mortality study is the attitude of some of the medical examiners toward performing autopsies on patients who die in childbirth.

The third patient was a twenty-seven-year-old primipara who was seen by her physician because of sudden severe pain in the right lower quadrant. Physical examination was negative. The pain increased during the next few hours, and the abdomen became distended; the patient went steadily downhill and died at home before the ambulance arrived. The diagnosis of ectopic pregnancy, as in the previous case, is the probable one; however, as neither operation nor autopsy was performed, it cannot be confirmed. In the absence of nausea and vomiting, and in view of symptomatology of so few hours' duration, hemorrhage was the most likely cause of death, and ectopic pregnancy the probable source of the hemorrhage.

The fourth patient, a thirty-eight-year-old multipara who had had one abortion at five months, was seized with sudden pain in the lower abdomen, accompanied by vaginal bleeding, when approximately eight weeks pregnant. After consultation, ruptured tubal pregnancy was diagnosed, and at operation the left tube was found to be ruptured and was removed. The patient was given one transfusion of 500 cc. of citrated blood, in spite of which she died about five hours after operation. Delayed operation was not a factor in this case, since the patient was operated on soon after the diagnosis had been made; it is possible that additional transfusions might have averted the catastrophe.

The fifth patient was a thirty-seven-year-old multipara on whom operation for repair of a rectocele and fixation of the uterus was performed. At operation a mass on the right side was found, which was said to have been a tubal pregnancy. Following this operation the patient became anuric and died. The description of the operation states that the uterosacral ligaments were plicated, and in all probability both ureters were involved in this operation, thus causing the anuria. Although this death is attributed to extrauterine pregnancy, which was an incidental finding at operation, the true cause was bungling surgery.

The sixth and final case was that of a thirty-nine-year-old primipara who was hospitalized for observation because of vaginal bleeding. Because the red-cell count fell very materially, operation was decided on. Ectopic pregnancy was found, and both tubes were removed because of extensive adhesions. The patient died three days later, probably because of bronchopneumonia. There is little to be said about this patient; she was apparently doing well from the surgical standpoint but expired because of a respiratory infection.

The two patients who died without operation show how serious the result of hemorrhage may be and how important it is that operation be performed whenever the diagnosis of ectopic pregnancy is suspected. This is the only way in which such fatalities can be prevented.

DEATHS

PETERSON — John A. Peterson, M.D., of Hingham, died December 26. He was in his seventy-third year.

Dr. Peterson attended Powers Institute and received his degree from the University of Vermont College of Medicine in 1896. For four years after his graduation he practiced in Guilford, Vermont. He then went to Hingham. He was former medical examiner of the Fifth Plymouth District and a former member of the Massachusetts Medical Society and the American Medical Association.

His widow and a daughter survive him.

STICKNEY — Edwin P. Stickney, M.D., of Arlington, died January 8. He was in his eighty-first year.

Dr. Stickney received his degree from Harvard Medical School in 1892. He was a fellow of the Massachusetts Medical Society and the American Medical Association. He was also a member of the New England Pediatric Society and the Arlington Doctors' Club.

Two daughters, a brother and three grandchildren survive him.

MISCELLANY

ELLA SACHS PLOTZ FOUNDATION

During the nineteenth year of the Ella Sachs Plotz Foundation for the Advancement of Scientific Investigation, forty-four applications for grants were received by the trustees, thirty-six of which came from the United States, the other eight coming from six different countries in Europe, Asia and North and South America. The total number of grants made during this year was twenty-six, one of these being a continued grant.

In the nineteen years of its existence the Foundation has made four hundred and fifty-five grants to scientists throughout the world.

In their first statement regarding the purposes for which the fund would be used, the trustees expressed themselves as follows:

> For the present, researches will be favored that are directed toward the solution of problems in medicine and surgery or in branches of science bearing on medicine and surgery.
>
> As a rule, preference will be given to researches on a single problem or on closely allied problems; it is hoped that investigators in this and in other countries may be found, whose work on similar or related problems may be assisted so that more rapid progress may be made possible.
>
> Grants may be used for the purchase of apparatus and supplies that are needed for special investigations, and for the payment of unusual expenses incident to such investigations, including technical assistance, but not for providing apparatus or materials which are ordinarily a part of laboratory equipment. Stipends for the support of investigators will be granted only under exceptional circumstances.

In the past few years the policy outlined in the second paragraph has been neglected. During the present great need for funds, grants will be given in the sciences closely related to medicine without reference to special fields. The maximum size of grants will usually be less than $500.

Applications for grants to be held during the year 1943–1944 must be in the hands of the Executive Committee before April, 1943. There are no formal application blanks, but letters asking for aid must state definitely the qualifications of the investigator, an accurate description of the research, the size of the grant requested and the specific use of the money to be expended. In their requests for aid, applicants should state whether or not they have approached other foundations for financial assistance. It is highly desirable to include letters of recommendation from the directors of the departments in which the work is to be done. Only applications complying with the above conditions will be considered.

Applications should be sent to Dr. Joseph C. Aub, Massachusetts General Hospital, Fruit Street, Boston.

CORRESPONDENCE

EXPECTORANTS

To the Editor: I have been interested in reading, in the September 3 issue of the *Journal*, the article on virus pneumonias by Drs. Dingle and Finland. There is one point brought out by these authors to which I wish to take exception. On page 384, they say, "Expectorants may be helpful when sputum is scant." If they refer to the commonly used stimulating expectorants, which act by virtue of the fact that they are excreted in the bronchi, the use of such drugs seems irrational. They are supposed to increase secretion by acting as irritants to the mucous membranes, where they are excreted. To irritate further an already inflamed mucous membrane does not seem likely to add to the comfort of the patient.

I am strongly inclined to believe that expectorants so used tend to increase cough in the acute stages of respiratory infections, and I have seen a number of cases of persistent cough and subacute cases that were promptly relieved when the patient stopped taking the expectorant.

GEORGE C. SHATTUCK, M.D.

25 Shattuck Street
Boston

* * *

Dr. Shattuck's letter was forwarded to Dr. Finland, whose reply is as follows:

To the Editor: According to my understanding, it is the purpose of an expectorant to decrease the viscosity of sputum and make it easier to raise, thus indirectly relieving the marked irritation that results from the difficulty in dislodging thick tenacious sputum during cough. Further relief from the irritation may be sought through the administration of generous doses of codeine or of suitable doses of such drugs as Dilaudid, if necessary. There is evidence to indicate that the viscosity of the tracheobronchial exudate is decreased by the usual expectorants and by the inhalation of moist air or mixtures of oxygen and small concentrations of carbon dioxide or compound tincture of benzoin (Basch, F. P., et al. *Am. J. Dis. Child.* **62**:981–990 and 1149–1171, 1941, and *J. A. M. A.* **117**:675–678, 1941; Nelson, E. E. *Internat. M. Digest* **40**:183–185, 1942).

Dr. Dingle and I were only too well aware of the frequent ineffectiveness of the usual measures. It must be borne in mind, however, that they are undertaken in the first place because the symptom is troublesome. Although Dr. Shattuck's experience may not be unique, the reverse is probably more frequently observed: that is, expectorants are withheld because relief from their use is not anticipated. The physician finally prescribes them in desperation, after which the patient begins to raise sputum more easily and with less irritation. Both these circumstances may, of course, be merely coincidences in the natural course of the disease. Two things are certain: severe and irritating cough is one of the most troublesome features of the prevalent primary atypical pneumonias, and the relief of this symptom is very difficult.

MAXWELL FINLAND, M.D.

Boston City Hospital
Boston

APPROVED LABORATORIES

To the Editor: In the October 8, 1942, issue of the *Journal*, a communication from this department was printed giving a list of the laboratories approved for performing premarital and prenatal serologic tests for syphilis.

Four laboratories have been added to this list, which brings the total to thirteen. The list is as follows:

State Wassermann Laboratory, Boston
Boston Dispensary, Boston
Boston Health Department, Boston
Leary Laboratory, Boston
Massachusetts General Hospital, Boston
Peter Bent Brigham Hospital, Boston
Health Department, Brockton
Truesdale Hospital, Fall River
Providence Hospital, Holyoke
St. Luke's Hospital, New Bedford
St. Luke's Hospital, Pittsfield
Mercy Hospital, Springfield
St. Vincent Hospital, Worcester.

Those sending such specimens to laboratories are reminded that no other laboratories in the State are approved for performing these tests.

PAUL J. JAKMAUH, M.D., *Commissioner*
Department of Public Health

State House
Boston

BOOK REVIEW

Manual of Standard Practice of Plastic and Maxillofacial Surgery. Prepared and edited by the Subcommittee on Plastic and Maxillofacial Surgery of the Committee on Surgery, Division of Medical Sciences, National Research Council, and representatives of the Medical Department, United States Army: Robert H. Ivy, M.D., chairman; John Staige Davis, M.D.; P. C. Lowery, M.D.; Joseph D. Eby, M.D.; Ferris Smith, M.D.; Brig. Gen. Leigh C. Fairbank, Medical Department U. S. A.; and Lt. Col. Roy A. Stout, D. C., U. S. A. With contributions of John Scudder, M.D., and Frederick P. Haugen, M.D. 8°, cloth, 432 pp., with 259 illustrations. Philadelphia: W. B. Saunders Company, 1942. $5.00.

The purpose of publishing a series of manuals on military surgery, of which this is the first one, is to present in compact form essential up-to-date and reliable information regarding military surgery to medical officers who are, by necessity, called on to treat the wounded under adverse conditions, as specialization cannot be followed to the same degree in military service as in civilian life. The degree of success of such a manual is proportional to the fulfillment of the above purpose, and so far as this book is concerned, the reviewer believes that it has fulfilled this requirement to a great degree.

The book is divided into four sections: reconstructive surgery (250 pages); maxillary surgery (79 pages); maxillofacial prosthesis (34 pages); and anesthetic technics (22 pages).

The section on reconstructive surgery is the most ambitious and thorough chapter. The author covers almost the entire field of plastic surgery. One is particularly impressed with the careful selection of plastic procedures, and the rejection of many complicated and unavoidable operations. It is well for military surgeons to pay special attention to the "don't's" that the author courageously emphasizes throughout the text. The greater part of this section is based on civilian types of injury. Although these are very useful and will undoubtedly act as a guide for the treatment of gunshot wounds, one would wish that the author had utilized part of the vast material published on this subject during World War I.

The section on maxillary surgery lays special emphasis on the early treatment of fractures, and outlines many useful suggestions and aids for emergency and first-aid immobilization of fractures.

The least impressive part is the section on maxillofacial prosthesis. It gives very little that the military dental surgeon can utilize for the treatment of the wounded.

The fourth section comprises two short chapters on the application of local and general anesthesia.

The book is well edited and contains many excellent diagrams and illustrations. It will undoubtedly be a useful reference book for those who are assigned to treat injuries of the face and jaws, as well as general injuries.

(Notices on page x)

MORALE IS A LOT OF LITTLE THINGS

(as you, Doctor, know better than most)

THERE'S BILL reading *that letter* again. What's in it? Well—"Katie had her birthday Thursday . . . Dad's an air-raid warden now . . . We're all going to the game tomorrow . . ."

Nothing very important—except to Bill.

But it's important to him all right—the way a lot of little things are to all of us. Letters from home . . . old friends . . . the pipe we smoke.

Little things that help to keep morale up!

* * *

It happens that millions of Americans attach a special value to their right to enjoy a refreshing glass of beer . . . in the company of good friends . . . with wholesome American food . . . as a beverage of moderation after a good day's work.

A small thing, surely—not of crucial importance to any of us.

And yet—morale is a lot of little things like this. Little things that help to lift the spirits . . . keep up the courage.

And, after all, aren't they among the things we fight for?

BREWING INDUSTRY FOUNDATION

NOTICES

ANNOUNCEMENT

Dr. William T. Hopkins announces a change of address from 1 Ocean Terrace, Lynn, to 103 Broad Street, Lynn.

SYMPOSIUM ON AVIATION MEDICINE

The medical director and the trustees of the Boston City Hospital, in an effort to comply with requests from representatives of the Medical Corps of the United States Army and Navy for the training of future medical officers for service with aviation units, will present a symposium on aviation medicine, under the auspices of the Department of Ophthalmology.

The sponsors hope that all potential medical officers of all services will take this opportunity to acquaint themselves with the medical problems of aviation. A cordial invitation to attend is therefore extended to members of the visiting staffs and house staffs of all hospitals, to other members of the medical profession and to all medical students. The lectures and demonstrations will be held in the Cheever Amphitheater of the Dowling Building, Boston City Hospital. Parking space within the hospital yard will be available; automobiles should enter through the Harrison Avenue gate.

Program

Sunday, January 17, 3:00 p.m.

The Role of the Medical Program in Civil Aviation. Ross A. McFarland, Ph.D., assistant professor of industrial research, Harvard University; co-ordinator of the Medical Program, Pan American Airways System.

Sunday, January 24, 3:00 p.m.

The Effects of High Altitude in Aviation. Ross A. McFarland, Ph.D.

Sunday, January 31, 3:00 p.m.

The Application of Psychiatry to the Military Needs. Commander A. Warren Stearns (MC), U.S.N.R.

The Application of Psychology to the Selection and Maintenance of Aircraft Pilots. Lieutenant Edward J. Galway, U.S.N.R.

Sunday, February 7, 3:00 p.m.

Naval Aviation. Captain J. C. Adams (MC), U.S.N., chief of the Division of Aviation, Bureau of Medicine and Surgery, United States Navy.

Demonstration of a Naval Flight Physical Examination. Lieutenant Commander L. R. Philbrook (MC), U.S. N.R., senior aviation examiner, First Naval District.

Sunday, February 14, 3:00 p.m.

Early Treatment of Traumatic Injuries of the Face and Jaw. Dr. V. H. Kazanjian.

Sunday, February 21, 3:00 p.m.

Head and Spinal Injuries. Dr. Donald Munro.

NEW ENGLAND OPHTHALMOLOGICAL SOCIETY

The annual meeting of the New England Ophthalmological Society will be held at the Massachusetts Eye and Ear Infirmary, 243 Charles Street, Boston, on Tuesday, January 19, at 8 p.m.

Following the business meeting, Dr. Hermann M. Burian and Dr. Kenneth N. Ogle of the Dartmouth Eye Institute will speak on the topic, "A Study of the Aniseikonia in a Case of Increasing Unilateral Index Myopia." The guest speaker, Dr. John H. Dunnington, professor of ophthalmology, Columbia University College of Physicians and Surgeons, will then speak on the subject, "Epidemic Keratoconjunctivitis."

HARVARD MEDICAL LECTURES

The faculty of the Harvard Medical School is giving a series of ten free, public lectures on medical subjects on Sunday afternoons in the amphitheater of the Peter Bent Brigham Hospital, starting at 4 o'clock.

The first two lectures, "The Role of the Endocrine Glands in Adaptation," by Dr. George W. Thorn, and "Newer Knowledge of Vitamins," by Dr. Joseph W. Ferrebee, were delivered on January 3 and 10, respectively. The subsequent lectures in the series will be as follows: January 17, "The Supply of Doctors," by Dr. Frank H. Lahey; January 24, "How Best to Eat under War Conditions," by Dr. Frederick J. Stare; January 31, "Common Colds and Their Complications," by Dr. Maxwell Finland; February 7, "The Care of Soldiers in an Army Hos-

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pital," by Lt. Col. Alexander Marble; February 14, "Problems of Ventilation in the Home," by Dr. Constantin P. Yaglou; February 21, "Civilian Physical Fitness as a War Measure," by Dr. Arlie V. Bock; February 28, "Healthy Children," by Dr. Allan M. Butler; and March 7, "Antiseptic and Chemotherapeutic Agents," by Dr. Rene J. Dubos. No tickets are required for admission.

CARNEY HOSPITAL

The monthly clinical meeting and luncheon of the staff of the Carney Hospital will be held in the auditorium of the Carney Hospital on Monday, January 18, at 11:30 a.m.

PROGRAM

Business.

Case reports: medical, surgical, obstetrical, gynecological, urological, orthopedic, ophthalmic, otolaryngological.

Physicians and medical students are invited to attend.

WILLIAM HARVEY SOCIETY

Dr. George W. Thorn, Hersey Professor of the Theory and Practice of Physic at Harvard Medical School, will speak on the topic, "The Clinical Aspects of Sodium and Chloride Metabolism," on Friday, January 22, at 8 p.m. in the auditorium of the Beth Israel Hospital. The William Harvey Society of Tufts College Medical School, which sponsors the lecture, invites all interested members of the profession to attend.

SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING SUNDAY, JANUARY 17

*3:00 p.m. The Role of the Medical Program in Civilian Aviation. Dr. Ross A. McFarland. Symposium on Aviation Medicine. Cheever Amphitheater, Dowling Building, Boston City Hospital.

†4:00 p.m. The Supply of Doctors. Dr. Frank H. Lahey. Amphitheater of the Peter Bent Brigham Hospital.

†5:00 p.m. Modern Medical Treatment of Acute and Chronic Alcoholism. Dr. Joseph Thimann. Washingtonian Hospital, 41 Waltham Street, Boston.

MONDAY, JANUARY 18

*11:30 a.m. Carney Hospital. Monthly clinical meeting and luncheon of the staff.

*12:15–1:15 p.m. Clinicopathological conference. Peter Bent Brigham Hospital amphitheater.

*8:15 p.m. New England Heart Association. Boston Medical Library, 8 Fenway.

TUESDAY, JANUARY 19

*9:00–10:00 a.m. Medical clinic. Dr. S. J. Thannhauser. Joseph H. Pratt Diagnostic Hospital.

*12:00 m. The Present Status of Physical Medicine in the Treatment of Rheumatoid Arthritis. Dr. Arthur L. Watkins. South End Medical Club. Headquarters of the Boston Tuberculosis Association, 554 Columbus Avenue, Boston.

*12:15–1:15 p.m. Clinicoroentgenologic conference. Peter Bent Brigham Hospital amphitheater.

8 p.m. New England Ophthalmological Society. Massachusetts Eye and Ear Infirmary, 243 Charles Street, Boston.

WEDNESDAY, JANUARY 20

*9:00–10:00 a.m. A Renal Complication of Sulfadiazine. Dr. Francis McDonald. Discussion by Dr. Edwin L. Prien. Joseph H. Pratt Diagnostic Hospital.

*12:00 m. Clinicopathological conference. Children's Hospital.

THURSDAY, JANUARY 21

*9:00–10:00 a.m. Medical clinic. Dr. S. J. Thannhauser. Joseph H. Pratt Diagnostic Hospital.

*4:00–5:00 p.m. Nutrition and Cardiac Disease. Dr. C. Sidney Burwell and Dr. Samuel A. Levine. Amphitheater, Peter Bent Brigham Hospital.

(Notices continued on page xiii)

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A Note Worth Reading

The advertising space in the *Journal* is your guarantee that the products you buy are of the highest quality. Only desirable firms are represented in these pages: they will continue to advertise only if you buy from them and thus prove to them that the *Journal* is the medical authority for reliable advertising.

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8:00 p.m. New England Pathological Society. Amphitheater, Peter Bent Brigham Hospital.

FRIDAY, JANUARY 22

*9:00–10:00 a.m. Clinicopathological conference. Dr. Henry R. Viets and Dr. H. E. MacMahon. Joseph H. Pratt Diagnostic Hospital.

*8:00 p.m. The Clinical Aspects of the Sodium and Chloride Metabolism. Dr. George W. Thorn. William Harvey Society. Auditorium, Beth Israel Hospital.

SATURDAY, JANUARY 23

*10:00–11:30 a.m. Medical staff rounds. Peter Bent Brigham Hospital.

*Open to the medical profession.

†Open to the public.

JANUARY 17–FEBRUARY 21. Symposium on Aviation Medicine. Page x.

JANUARY 17–FEBRUARY 28. Harvard Medical lectures. Page x.

FEBRUARY 13. American Board of Obstetrics and Gynecology. Page 690, issue of October 29.

DISTRICT SOCIETIES

BRISTOL SOUTH

MAY 6. New Bedford.

ESSEX NORTH

MAY 5.

ESSEX SOUTH

FEBRUARY 3. Lynn Hospital.

MARCH 3. Essex Sanatorium.

APRIL 7. Addison Gilbert Hospital, Gloucester.

MAY 5. Salem Country Club.

FRANKLIN

MARCH 9.

MAY 11. Annual meeting.

All meetings are held at 11:00 a.m. at the Franklin County Hospital, Greenfield.

HAMPSHIRE

MARCH 3.

MAY 5.

MIDDLESEX EAST

JANUARY 27.

MARCH 17.

MAY 5.

All meetings are held at the Bear Hill Golf Club, Stoneham, at 12:15 p.m., except that of May 5, which will be held at 6:30 p.m.

MIDDLESEX NORTH

JANUARY 27.

APRIL 28.

JULY 28.

PLYMOUTH

JANUARY 21. Brockton Hospital.

FEBRUARY 18. Jordan Hospital, Plymouth.

MARCH 18. Goddard Hospital.

APRIL 15. Bridgewater State Farm.

MAY 20. Lakeville.

WORCESTER

FEBRUARY 10. Worcester State Hospital, Worcester.

MARCH 10. Memorial Hospital, Worcester.

APRIL 14. Hahnemann Hospital, Worcester.

MAY 12. Annual meeting.

WORCESTER NORTH

JANUARY 27.

APRIL 28.

JULY 28.

Washingtonian Hospital

41 WALTHAM STREET, BOSTON, MASS.
Founded 1841
A nonprofit-making, endowed institution, reorganized, for the
MODERN TREATMENT OF MEN SUFFERING FROM ACUTE OR CHRONIC
ALCOHOLISM
JOSEPH THIMANN, M.D., *Medical Superintendent*
MERRILL MOORE, M.D., *Director of Research*
Visits by Psychiatric and Neurological Staff
Consultants in Medicine, Surgery and the Specialties
Rates Moderate
For information: consult the Medical Superintendent
Telephones: HAN 1750 and 1751

Channing Sanitarium

ESTABLISHED 1879

A pleasant country community of cottages built for the homelike care and treatment of nervous patients. Separate cottage for the care of convalescent nonmental patients. Occupational therapy. Tennis court. Sports building.

JACKSON M. THOMAS, M.D., *Superintendent*
CLIFFORD G. ROUNSEFELL, M.D., *Resident Physician*

WELLESLEY, MASSACHUSETTS
Telephone — Wellesley 0464

Bournewood Hospital

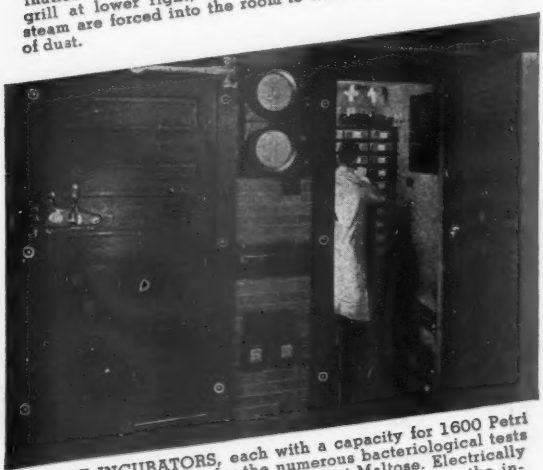
300 SOUTH STREET, BROOKLINE, MASS.
Established 1884
For a limited number of cases of mental and nervous diseases
POST OFFICE, CHESTNUT HILL
Telephone PAR 0300
GEORGE H. TORNEY, M.D.

CHARLES B. TOWNS HOSPITAL

Serving the Medical Profession for Over 40 Years
FOR ALCOHOLISM AND DRUG ADDICTION EXCLUSIVELY
Definite Treatment -- Fixed Charges -- Minimum Hospitalization
293 CENTRAL PARK WEST, NEW YORK, N. Y. -- Tel: SChuyler 4-0770
(*Hospital Literature*)

STEAM-WASHED PLATING ROOM where bacteriological analyses are made with every precaution to prevent contamination. All air taken into this glassed-in room is filtered (see grill at lower right) and, at intervals as required, jets of steam are forced into the room to wash the atmosphere free of dust.

THE EUSCOPE enables the bacteriologist to study microscopic subjects for long periods in easily visible form. Essentially a micro-projection apparatus, the euscope enlarges the microscopic image and thus makes for greater accuracy. Used with a screen it enables the operator to demonstrate specimens to a group.



LARGE INCUBATORS, each with a capacity for 1600 Petri dishes, offer facilities for the numerous bacteriological tests made daily to assure the purity of Dextri-Maltose. Electrically heated and equipped with recording thermometers, the incubators can be varied from room temperature to 60° C. Uniform temperature is maintained within ± 1 degree.

BOTTLE-FILLER developed in and reported from the Mead Johnson Laboratory to expedite bacteriological procedures and so to give time for more tests. Filling the bottles with distilled water, a stage in testing samples, formerly required several hours but is now reduced to a fraction of that time.

Only the

Most Modern Equipment for Testing DEXTRI-MALTOSE

EVERY type of equipment conducive to speed and accuracy in bacteriological tests is available in the Mead Johnson Laboratory. Steam- and electrically-heated sterilizers are automatically controlled. One of the newest has a capacity of 75 liters of media and required installation of a special steam-line. Besides the large incubators shown above, the laboratory has a number of smaller ones which, together with cold storage rooms, permit any desired temperature from –20° to 80° C. There is complete centrifuge equipment, including a supercentrifuge with a capacity of 40,000 R.P.M. Small equipment is of similar high standard — precision glassware for measuring and sensitive balances for weighing, as examples. All these facilities, together with many others, have been proved worth while for sanitary control in infant feeding, as is shown by a quarter of a century of experience.

"The True Measure of Economy is Value, Not Price"

SANITARY CONTROL OF DEXTRI-MALTOSE . . . (NO. 6 OF A SERIES)